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THE EFFECTS OF TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION ON NERVE CONDUCTION VELOCITY, GRIP STRENGTH, PAIN, AND UPPER EXTREMITY FUNCTIONALITY IN INDIVIDUALS WITH CARPAL TUNNEL SYNDROME

ORIGINAL ARTICLE

ABSTRACT

Purpose: This study aims to investigate the effects of transcutaneous auricular vagus nerve stimulation (taVNS) on key parameters, including nerve conduction velocity, grip strength, pain, and upper extremity functionality in individuals with carpal tunnel syndrome (CTS).

Methods: The study involved 51 patients (90 hands) diagnosed with carpal tunnel syndrome, comprising 12 males and 39 females, ranging in age from 18 to 58 years. Participants were divided into groups by random randomization method. Sensory branch conduction velocity of the median nerve was assessed via electromyography (EMG), hand grip strength was measured using a digital dynamometer, and pain intensity was quantified with a visual analog scale (VAS); additionally, upper extremity functionality was evaluated using the Upper Extremity Functional Index (UEFI) scale before and after the treatment. In the experimental group, in addition to the conventional physiotherapy program, 10 sessions of auricular vagus nerve stimulation were administered; for the sham and control groups, the conventional physiotherapy program alone was conducted over the course of 10 sessions.

Results: The analysis revealed no statistically significant differences between the groups concerning variables such as body mass index (BMI), age, gender, educational background, and smoking status ($p>0.05$). However, within-group evaluations exhibited significant differences compared to baseline values in terms of nerve conduction velocity, pain perception, and upper extremity functionality, with no such difference observed in grip strength ($p<0.05$). The intergroup comparisons indicated a significant difference in favor of the experimental group across all parameters, except for grip strength ($p<0.05$); conversely, no substantial differences were observed between the sham and control groups ($p>0.05$).

Conclusion: The findings suggest that the adjunctive use of taVNS alongside conventional rehabilitation programs in individuals diagnosed with CTS results in increased sensory nerve conduction velocity and enhanced upper extremity functional capacity, accompanied by a reduction in pain; nevertheless, grip strength remains unaffected.

Keywords: Cranial Nerve X, Carpal Tunnel, Nerve Conduction Studies

KARPAL TÜNEL SENDROMU TANILI BİREYLERDE TRANSKÜTANÖZ AURİKÜLER VAGUS SİNİR UYARIMININ SİNİR İLETİ HIZI, KAVRAMA KUVVETİ, AĞRI VE ÜST EKSTREMİTE FONKSİYONELLİĞİNE ETKİSİ

ARAŞTIRMA MAKALESİ

ÖZ

Amaç: Transkütanöz auriküler vagus uyarımının(taVNS) KTS'de sinir ileti hızı, kavrama kuvveti, ağrı ve üst ekstremite fonksiyonelliği gibi parametrelerdeki etkisinin araştırılması amaçlanmaktadır.

Yöntem: Çalışmaya karpal tünel sendromu tanısı almış, yaşları 18-58 aralığında değişen 51 hasta (90 el) 12 erkek 39 kadın dahil edilmiştir. Katılımcılar, rastgele randomizasyon yöntemi ile gruplara ayrılmışlardır. Tedavi öncesi ve sonrasında olacak şekilde median sinirin duyusal dalının ileti hızını ölçmek amacı ile elektromyografi (EMG) değerlendirmesi, bir dijital dinamometre yardımı ile el kavrama kuvveti, vizüel analog skalası (VAS) ölçeği ile ağrı sorgulaması ve üst ekstremitenin fonksiyonelliğini ölçmek amacı ile üst ekstremite fonksiyonel indeksi (ÜEFİ) ölçeği uygulanmıştır. Çalışmada yer alan deney, sham ve kontrol gruplarına konvansiyonel fizyoterapi programı 10 seans olacak şekilde uygulanırken, deney grubuna konvansiyonel fizyoterapi programıyla birlikte ek olarak 10 seans auriküler vagus sinir uyarımı da gerçekleştirilmiştir.

Sonuçlar: Çalışmada gruplar arasında VKİ, yaş, cinsiyeti eğitim durumu, sigara kullanma durumu gibi parametreler açısından anlamlı farklılıklar bulunmamıştır ($p>0,05$). Grup içi yapılan değerlendirmelerde kavrama kuvveti dışında kalan sinir ileti hızı, ağrı ve üst ekstremite fonksiyonelliği açısından başlangıç durumuna göre anlamlı farklılık bulunmuştur ($p<0,05$). Grupların karşılaştırılması için yapılan analizde ise kavrama kuvveti parametresi dışında kalan tüm parametrelerde deney grubu lehine anlamlı farklılık bulunurken ($p<0,05$), sham ve kontrol grupları arasında anlamlı bir farklılık bulunmamıştır ($p>0,05$).

Tartışma: Çalışma sonucunda KTS tanısı almış bireylerde konvansiyonel rehabilitasyon programına ek olarak uygulanan taVNS'nin duyusal sinir ileti hızını ve üst ekstremite fonksiyonellik seviyesini yükselttiği, ağrıyı azalttığı ancak kavrama kuvveti üzerinde herhangi bir etki oluşturmadığı bulunmuştur.

Anahtar Kelimeler: X. Kranial Sinir, Karpal Tünel, Sinir İleti Çalışmaları

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INTRODUCTION

Peripheral nerves travel alongside various anatomical structures. The interaction between nerves and surrounding structures can lead to nerve compression. This is referred to as 'entrapment neuropathy.' Entrapment neuropathies give rise to symptoms such as pain, numbness, and tingling due to the nerves being impacted. The degree of compression on peripheral nerves can vary. The most prevalent type of entrapment neuropathy is median nerve neuropathy (1).

The median nerve follows a route through a passage formed by the carpal bones and carpal ligament at the wrist level. Changes in this tunnel can result in compression of the median nerve. This condition is known as carpal tunnel syndrome (CTS). Much like other entrapment neuropathies, CTS manifests as symptoms including pain and numbness along the nerve's course (2, 3).

Although the primary cause of CTS remains unclear, several factors are considered to contribute to its manifestation. Generally, three pathoanatomical factors are involved in the emergence of CTS. These factors include elevated pressure within the carpal tunnel, ischemic nerve changes, and compression from adjacent structures (4).

The diagnostic assessment should be comprehensive for CTS diagnosis. This assessment begins with a patient history. It should be followed by an extensive physical examination conducted by specialized physicians. In addition, electrophysiologic tests, imaging modalities, and provocative tests should also be included in the diagnostic assessment (5). Despite these assessments, sensitivity is not 100%. In addition, there is no consensus on which diagnostic criteria are most suitable (2, 6).

Numerous treatment modalities are available for CTS. The choice of treatment differs among individuals. Individual characteristics, the extent of median nerve damage, the accessibility of the treatments to be used, and the efficacy of the selected treatment method are important in developing the treatment plan (7, 8).

The primary objective of treatment methods applicable to CTS is the alleviation of pressure on the median nerve. In this regard, both surgical and conservative treatment approaches are considered. Electrophysiologic parameters play a pivotal role in the classification of treatment methods, with conservative approaches typically recommended for mild and moderately affected individuals, while surgical interventions are usually indicated for advanced and severe CTS cases (9).

Conservative treatment methodologies include splinting, prescribed exercises, medications, electrotherapy, and other physical therapy modalities (10). Notably, non-invasive vagus nerve stimulation, which has gained prominence in recent years, has demonstrated its efficacy in musculoskeletal conditions (11).

Our study postulates that transcutaneous auricular vagus nerve stimulation (taVNS) will result in increased nerve conduction velocity, enhanced grip strength, reduced pain levels, and improved upper extremity functionality among individuals diagnosed with mild to moderate carpal tunnel syndrome.

METHODS

This study employed a randomized controlled clinical research design, utilizing pre- and post-test assessment methodologies. A total of 51 patients, representing 90 hands, all diagnosed with CTS, were included as participants in this study. Before starting the research, ethical approval was obtained from the Ethics Committee for Scientific Research and Publication at Artvin Çoruh University, with approval granted on March 2, 2022, under reference no: E-18457941-050.99-41587. All participating individuals were informed about the research, and their informed consent was obtained through the signing of a "Voluntary Consent Form."

Inclusion Criteria: Aged 18 years or older, voluntarily agreeing to participate in the study., providing informed consent by signing the voluntary consent form., diagnosis of CTS within the mild to moderate classification.

Exclusion criteria: Participants who are unwilling to continue in the study, pregnancy or suspected pregnancy, injuries that could occur during the treatment of the upper or lower extremities, acute wounds or ear infections, exposure to severe trau-

ma affecting the upper extremities and cervical spine during the study, patients who missed treatment sessions.

Study Plan

Power and sample size calculations were conducted using G*Power version 3.1 software (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). To achieve a power of 0.80 with an effect size of 0.80, a total of 75 hands were required for recruitment. Eligible participants were provided with comprehensive explanations regarding the study methods and procedures. Following these explanations, individuals who voluntarily consented to participate and signed the informed consent form were included in the study. Participants were asked to complete a personal information form, which included details about age, gender, body mass index, educational background, smoking status, and dominant hand; subsequently, the participants were randomly assigned to one of three groups. To implement this methodology, three envelopes were provided to participants. Each envelope has a number enclosed. Participants were assigned to one of the three groups based on the number they randomly drew: 1-experiment group, 2-sham group, or 3-control group. The envelope belonging to the group with the completed number of participants was removed and randomization was carried out in this way until the groups were completed. All groups received a 10-session conventional physiotherapy program consisting of transcutaneous electrical nerve stimulation (TENS), ultrasound applications, stretching exercises, and mobilizations. However, the experiment group received an additional ten sessions of taVNS in conjunction with the conventional physiotherapy program, while the sham group underwent sham taVNS application involving the use of headphones for auricular vagus stimulation without the application of current. Adherence to the principles outlined in the Declaration of Helsinki was maintained throughout the study.

Assessment parameters

Demographic information. A questionnaire was administered to gather demographic data from participants, including details such as age, gender, body mass index, educational background, and smoking habits.

Nerve Conduction Velocity Assessment: In accordance with the recommendations of the American Electrodiagnostic Medical Association, EMG is used to diagnose CTS. Standardised electrophysiological parameters for CTS are nerve conduction studies and needle electromyography methods (12, 13). The sensitivity of electrophysiological tests has a range of 56-85% and specificity is over 94%. This has made EMG evaluation a gold standard for the diagnosis of CTS (14). Electromyography was conducted by the same technician in a hospital setting to assess nerve conduction velocity in all participants. During this examination, participants were seated, and electrodes were positioned as required for median nerve measurements. Electroneurophysiological tests were carried out utilizing a 2-channel Alpin-Biomed device. Subsequently, the results were forwarded to a specialist for diagnosis.

Grip Strength Measurement: To measure grip strength, a Cambry dynamometer was used. Participants sat in chairs with their shoulders slightly abducted and in a neutral position, elbows flexed at 90°, and forearms and wrists in a neutral position. Three consecutive tests were performed while participants remained seated. One-minute intervals were allocated between each test. The mean scores of the three measurements were used in statistical analysis (15).

Pain Assessment: Pain levels were evaluated using the Visual Analog Scale (VAS). This scale consists of a 10 cm line, with “0” at one end representing the absence of pain and “10” at the opposite end signifying unbearable pain. Patients were provided with explanations regarding these endpoints and asked to mark the point on the scale that best described their current pain level (16).

Upper Extremity Functional Status Assessment: The Upper Extremity Functional Index (UEFI) was employed to assess the functional status of the upper extremities. The Turkish version of this scale, adapted by Aytar et al., comprises a total of 15 items aimed at measuring functional status. Each item offers five options to gauge the level of difficulty. Participants indicated their most suitable choice and the resulting scores were assessed (17).

Table 1. Comparison of Socio-Demographical Characteristics of Experimental, Sham and Control Groups

		Experimental Group (n:16 patients (30 hands))		Sham Group (n:18 patients (30 hands))		Control Group (n:17 patients (30 hands))		Test Value and Significance
Age	**Mean±SD** **Median (Min-Max)**	47.37±5.82 46.50 (38-58)		47.23±4.95 47 (38-56)		46.70±5.21 47.50 (36-55)		F: 1.12 p: 0.32
BMI	**Mean±SD** **Median (Min-Max)**	32.19±2.35 32.45 (27.30-36.80)		31.22±3.29 31.1 (26.50-36.60)		31.75±2.79 31.10 (26.50-36.80)		x^2: 1.56 p: 0.45
		Number (n)	**Percentage (%)**	**Number (n)**	**Percentage (%)**	**Number (n)**	**Percentage (%)**	
Gender	Male	3	18.75	5	27.77	4	23.52	x^2: .38 p: 0.82
	Female	13	81.25	13	72.23	13	76.48	
Education Level	Primary	9	56.25	10	55.55	10	58,82	x^2: 97 p: 0.98
	Secondary	4	25	5	27.77	4	23.52	
	High school	2	12.50	1	5.55	2	11.76	
	University	1	6.25	2	11.13	1	5.90	
Smoking status	Yes	3	18.75	4	22.22	4	23.52	x^2: .11 p:0 94
	No	13	81.25	14	77.78	13	76.48	

BMI:Body Mass İndex F: One-Way ANOVA Test. x^2: Chi-Square Test

Statistical analysis

Analysis of the data collected was conducted using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). in this study. The normality distribution of the data was assessed with the Shapiro-Wilk test; for the data conforming to a normal distribution, parametric analyses were employed, while non-parametric analyses were used for non-normally distributed data. Within-group comparisons of pre- and post-test results were made using the Wilcoxon Signed Rank Test and Paired Samples t-test; to compare pre- and post-test data between groups, as well as age and BMI values among groups, Kruskal Wallis H and One Way ANOVA analyses were applied. Gender, educational status, and smoking status were compared between groups using Chi-squared analysis (18).

RESULTS

There were no statistically significant differences observed among the groups in terms of mean age, BMI, gender distribution, educational levels, and smoking status (p>0.05) (Table 1).

Table 2. Comparison of Pre-Test and Post-Test EMG, Grip Strength, VAS and UEFI Measurement Results of the Experimental Group

	Mean±SD **Median (Min-Max)**		**z value**	**p value**
	Pre Test (n:16 patients (30 hands)	**Post Test (n:16 patients (30 hands)**		
Sensory Nerve Conduction Velocity (m/s)	41.05±2.75 41.30 (35.4-45.3)	45.64±2.55 45.75 (40.8-49.2)	-4.78	0.00***
VAS	6.33±0.84 6 (5-8)	3.03±0.72 3 (1-4)	-4.83	0.00***
Function (UEFI)	29.40±2.67 30 (24-33)	36.93±0.91 37 (35-38)	-4.79	0.00***
	Mean±SD **Median (Min-Max)**		**t value**	**p value**
	Pre Test (n:16 patients (30 hands)	**Post Test (n:16 patients (30 hands)**		
Grip strength (kg)	28.76±1.64 28.5 (26.10-31.60)	29.30±1.87 29.25 (24.6-31.7)	-1.601	0.10

VAS:Visuel Analog Scale UEFI: Upper Extremity Fonctional İndex z: Wilcoxon Signed Ranks Test. ***p<0.001, z: Paired Samples T Test.

Table 3. Comparison of Pre-Test and Post-Test EMG, Grip Strength, VAS and UEFI Measurement Results of the Sham Group

	Mean±SD Median (Min-Max)		t value	p value
	Pre Test (n:16 patients (30 hands)	**Post Test (n:16 patients (30 hands)**		
Sensory Nerve Conduction Velocity (m/s)	40.40±2.93 40.35 (35.3-45.7)	40.96±3.02 41.40 (34.2-46.9)	-2.575	0.01*
	Mean±SD Median (Min-Max)		**z value**	**p value**
	Pre Test (n:16 patients (30 hands)	**Post Test (n:16 patients (30 hands)**		
Grip strength (kg)	29.03±1.58 28.75 (26.90-31.60)	29.57±1.90 29.25 (26.20-33.20)	-1.34	0.18
VAS	6.10±0.76 6 (5-8)	3.47±0.57 3 (3-5)	-4.89	0.00***
Function (UEFI)	28.97±2.68 29 (24-33)	35.97±1.30 36 (34-38)	-4.79	0.00***

VAS: Visuel Analog Scale z: Paired Samples T Test. *p<0.05, z: Wilcoxon Signed Ranks Test.

Within the experimental group, pre-test and post-test values were analyzed. The results of the analysis indicated a statistically significant difference in EMG findings, which assessed the nerve conduction velocity of the sensory branch of the median nerve, VAS pain scores, and UEFI values, reflecting the functional status of the upper extremity (p<0.05) (Table 2).

Within the sham group, pre-test and post-test values were compared. The results of the analysis indicated a statistically significant difference in EMG findings, which assessed the nerve conduction velocity of the sensory branch of the median nerve, VAS pain scores, and UEFI values, reflecting the functional status of the upper extremity (p<0.05) (Table 3).

Within the control group, pre-test and post-test values were compared. The results of the analysis indicated a statistically significant difference in EMG findings, which assessed the nerve conduction velocity of the sensory branch of the median nerve, VAS pain scores, and UEFI values, reflecting the functional status of the upper extremity (p<0.05) (Table 4).

Upon analyzing the intergroup differences, statistically significant differences were identified among

Table 4. Comparison of Pre-Test and Post-Test EMG, Grip Strength, VAS and UEFI Measurement Results of the Control Group

	Mean±SD Median (Min-Max)		t value	p value
	Pre Test (n:17 patients (30 hands)	**Post Test (n:17 patients (30 hands)**		
Sensory Nerve Conduction Velocity (m/s)	41.40±2.06 41.20 (37.30-45.30)	42.11±2.28 42.55 (35.90-45.70)	-2.326	0.02*
	Mean±SD Median (Min-Max)		**z value**	**p value**
	Pre Test (n:17 patients (30 hands)	**Post Test (n:17 patients (30 hands)**		
Grip strength (kg)	28.68±2.10 28.65 (23.80-31.90)	28.76±2.31 28.70 (21.10-33.10)	-.535	0.59
VAS	6.40±0.86 6 (5-8)	3.43±0.57 3 (2-4)	-4.941	0.00***
Function (UEFI)	28.90±2.55 29 (24-33)	36.13±1.33 36 (34-38)	-4.795	0.00***

VAS:Visuel Analog Scale UEFI: Upper Extremity Fonctional İndex z: Paired Samples T Test. *p<0.05, z: Wilcoxon Signed Ranks Test.

Table 5. Comparison of Pre-Test and Post-Test EMG Measurement Results of Experimental, Sham and Control Groups

		Mean±SD Median (Min-Max)			F/x² value	p value
		Experimental Group (n:16 patients (30 hands))	Sham Group (n:18 patients (30 hands))	Control Group (n:17 patients (30 hands))		
Sensory Nerve Conduction Velocity (m/s)	Pre-Test	41.05±2.75 41.30 (35.40-45.30)	40.40±2.93 40.35 (35.30-45.70)	41.40±2.06 41.20 (37.30-45.30)	1.12F	0.32
	Post Test	45.64±2.55 45.75 (40.80-49.20)	40.96±3.02 41.40 (34.20-46.90)	42.11±2.28 42.55 (35.90-45.70)	32.708x2	0.00***

F: One-Way ANOVA Test. x^2: Kruskal-Wallis H Testi. ***p<0.005

the groups concerning nerve conduction velocity, pain, and upper extremity functionality, whereas no significant differences were observed regarding muscle strength. The difference between the groups is in favour of the experimental group. While the experimental group showed a significant difference compared to the sham and control groups, no significant difference was found between the sham and control groups (Table 5).

DISCUSSION

This study was carried out to investigate the effect of auricular vagus nerve stimulation on nerve conduction velocity, pain, grip strength and upper extremity functionality in individuals diagnosed with carpal tunnel syndrome. The study is one of the first studies in the literature and aims to develop a new treatment method in the clinic.

CTS is characterized by a constellation of symptoms resulting from the compression of the median nerve at the carpal tunnel level. The predominant clinical manifestations include pain, numbness, and tingling (2, 19, 20).

Common symptoms in CTS, such as hand paresthesia and morning pain are primarily attributed to local inflammation and tenosynovitis of the finger flexors, leading to damage of the median nerve. This damage is caused by carpal tunnel stenosis, the anatomical structures surrounding the median nerve, and the considerable mobility of the wrist. These factors lead to prolonged venous stasis, ischemia, and edema, collectively affecting the structure and function of the median nerve and subsequently elevating the pressure within the carpal tunnel (5, 21).

In CTS, edema tends to predominantly affect sensory nerve fibers, while ischemia exerts a greater impact on nociceptive fine fibers. Alterations in wrist positioning can further aggravate inflammation and ischemia within the carpal tunnel. Techniques aimed at alleviating venous stasis and edema, and effectively reducing pressure within the carpal tunnel, are regarded as beneficial maneuvers for addressing this condition (22).

In recent years, the use of taVNS has gained momentum as a therapeutic approach with such effects. The vagus nerve is recognized as a key regulator of the parasympathetic nervous system, an autonomic nervous system division However, it is known as a modulator of inflammation (23, 24). This role is achieved through the release of acetylcholine and its binding to acetylcholine receptors. However, nicotinic receptors have also been identified as influential in controlling systemic inflammation (25). Beyond this, the vagus nerve is also effective in pain modulation. Given these two attributes, vagus nerve stimulation has started to be explored as a novel therapeutic approach with potential applications in conditions such as inflammatory bowel diseases and musculoskeletal disorders (26, 27).

Early studies into the anti-inflammatory potential of vagus nerve stimulation focused on patients with epilepsy. As a result, research demonstrated that VNS contributes to the reduction of serum interleukin-6 (IL-6) levels while elevating the interleukin-10 (IL-10) levels (28, 29). Furthermore, VNS has also been proven to decrease the production of interleukin-8 (IL-8), tumor necrosis factor (TNF), interleukin-1B (IL-1B), and interleukin-6 (IL-6) (24, 30). In addition, vagus nerve stimulation can attenuate neuronal damage through shared cholinergic anti-inflammatory pathways (31, 32).

An investigation was carried out to assess the impact of vagus nerve stimulation on peripheral neuropathies. The study involved the classification of

rats into four distinct groups, namely: control, VNS, sham surgery, and chemotherapy-induced peripheral neuropathy (CIPN). In the CIPN, sham surgery, and VNS groups, rats received intraperitoneal injections of 2 mg/kg paclitaxel on separate days, while the control group was administered saline. On the first day, the sham surgery group underwent a sham surgical procedure. The VNS group, on the other hand, received vagus nerve stimulation, while no interventions were performed on the control and CIPN groups. Various behavioral tests, western blotting assays, and immunohistochemistry assessments were performed throughout the study. The results indicated a significant reduction in withdrawal latency due to paclitaxel treatment. This reduction was more pronounced in the VNS group when compared to the sham surgery group. However, the VNS group displayed no alterations in the expression of nuclear factor-kappa B (NF-κB) or tumor necrosis factor-alpha (TNF-α) compared to untreated rats, while interleukin-10 (IL-10) levels were notably upregulated (33).

In a separate study involving rats, the effects of VNS on neurodegenerative conditions and motor symptoms were examined. The rats were categorized into five groups: control, lesion, lesion+low frequency VNS, lesion+high frequency VNS, and lesion+microburst biomimetic VNS. In the study, daily locomotor activities, forelimb akinesia, the number of TH-positive neurons in the LC-NE system, impacts on the substantia nigra dopaminergic (SN-DA) system, and neuroinflammation were assessed. The findings of the study demonstrated that locomotor activity levels, forelimb akinesia, the number of TH-positive neurons in the LC-NE system, effects on the SN-DA system, and neuroinflammation were restored to baseline values in all groups. However, the groups receiving VNS had more significant improvements compared to the other groups. These results suggest that VNS could effectively impede disease progression by targeting degeneration mechanisms rather than solely addressing symptom management (34).

Conclusion

In our study, we conducted a comparative analysis among the experimental, sham, and control groups to evaluate the efficacy of the intervention under investigation. This analysis revealed a significant difference favoring the experimental group in parameters related to sensory branch nerve conduction velocity, pain levels, and upper extremity functionality; whereas, no significant difference was observed between the sham and control groups. In addition, our comparisons did not reveal any significant difference among the groups concerning grip strength. Upon careful examination of the findings, it becomes evident that individuals diagnosed with CTS experience a notable impact on their upper extremity functionality. This impact can also affect their professional, social, and physical well-being. We propose that the use of taVNS may hold promise in the treatment of these symptoms.

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