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ROLE OF TRANSCUTANEOUS VAGUS NERVE STIMULATION IN UPPER LIMB REHABILITATION IN PATIENTS WITH STROKE - A NARRATIVE REVIEW

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ABSTRACT

Background: Stroke significantly impacts an individual's physical, cognitive, and emotional well-being . Stroke occurs when blood supply of the brain is interrupted or reduced, preventing brain tissue from getting oxygen and nutrients. There are two main types of stroke, Ischemic Stroke (most common – about 87% of strokes) Caused by blockage of blood flow to the brain. Haemorrhagic Stroke Caused by bleeding into or around the brain. Vagus Nerve Stimulation (VNS) is a therapeutic approach that involves delivering electrical impulses to the vagus nerve for improvement in motor pathways to brain, motor recovery in upper extremity and enhance the neuroplasticity in brain. While the physiotherapeutic exercise protocol remain the primary treatment for the patient with stroke, VNS has shown potential to regain in the lost motor and sensory function of upper extremity, improvement in performance of ADLs and quality of life in patients with stroke . This review aimed to explore the role of transcutaneous vagus nerve stimulation (t-VNS) in upper limb dysfunction in patient with stroke. **Methods:** A brief review of the literature was conducted using PubMed, Google Scholar, and Research Gate databases, restricted to trials published in English-language only in last decade. Of the 116 articles retrieved, 10 were included in the review. **Results:** The results revealed that t-VNS combined with other physiotherapeutic interventions was effective in improving stroke related neurological deficits, degree of disability, dependence in performing ADLs, enhancing emotional well-being, life satisfaction, and quality of life in patient with stroke. **Conclusions:** t-VNS paired with traditional physiotherapy or other rehabilitation methods can enhance stroke related neurological deficits, level of disability and improve quality of life in patients with stroke.

KEYWORDS

Stroke, Upper Limb Dysfunction and Transcutaneous Vagus Nerve Stimulation

INTRODUCTION

Stroke is defined as a neurological impairment resulting from an acute, localized injury to the central nervous system due to vascular events, such as cerebral infarction, intracerebral haemorrhage, and subarachnoid hemorrhage.[1] It is the leading cause of disability and mortality worldwide.[2] According to the 2021 Global Burden of Disease report, ischemic stroke continues to present a significant global health burden, with its worldwide incidence significantly increased since 1990.[2]

The vagus nerve is a mixed cranial nerve that plays a vital role in the parasympathetic nervous system, influencing several body systems including cardiovascular, gastrointestinal, and respiratory functions.[3] VNS is a therapeutic technique that involves delivering electrical impulses to the vagus nerve to modulate its neural activity. VNS has shown potential in enhancing neurological function and promoting recovery in patients with stroke, by influencing brain regions involved in motor control and neuroplasticity.[4] VNS is of two types invasive and non-invasive.[3]

For invasive VNS, a programmable signal generator is implanted in the patient's upper left chest. This device emits charge-balanced waveforms at a constant current and is designed to deliver controlled electrical stimulation. The battery life of the generator depends on the generator model, the programmed stimulation parameters and the lead impedance values of the stimulation electrode.[5] The stimulation delivered through this device can help in modulating activity in areas of the brain responsible for motor recovery and neurological function after stroke.[4] When a new battery is required, the whole generator is replaced to prevent opening the hermetically sealed titanium case and to avoid contact between body fluids and generator components with the risk of inducing a rejection reaction, this procedure lead to a high chance of complications.[5]

In contrast to invasive methods, transcutaneous vagus nerve stimulation (t-VNS) is a non-invasive approach that delivers electrical stimulation through the skin. The outer ear, specifically the cymba conchae, serves as the main target site for t-VNS due to its predominant innervation by the auricular branch of the vagus nerve (ABVN), making it the ideal site for stimulation. This approach is safer compared to invasive VNS.[6]

To apply t-VNS, specialized earphones or devices equipped with dot-like electrodes are positioned on the left auricular cymba conchae. The stimulation is administered at a level above the sensory detection threshold but below the pain threshold, ensuring the patient perceives the stimulus without discomfort. This targeted stimulation generates specific patterns of brain activation related to sensorimotor processing and neuroplasticity.[7] t-VNS is found effective in enhancing neuroplasticity, thereby aiding in the functional recovery of stroke survivors. It has shown particular promise in individuals with motor and sensory impairments, improving outcomes such as upper limb function, spasticity, motor performance, and psychological well-being, improving life satisfaction and quality of life In patient with stroke.[4]

Exploring the effectiveness of t-VNS in improving upper limb dysfunction and motor abilities, can help find an effective intervention for improving upper extremity rehab outcomes in patients with stroke. Therefore, this review aimed to explore the role of transcutaneous vagus nerve stimulation (t-VNS) in improving upper limb dysfunction in patients with stroke.

METHODS

Relevant Literature was searched in Google scholar, PubMed, Research Gate databases and Cochrane Library restricted to English language articles published within the last ten years, using keywords “stroke”, “upper limb dysfunction”, “upper limb motor function” and “non-invasive vagus nerve stimulation”. One hundred six articles were retrieved. Ten articles were included in the review.

Table 1: Summary of the Studies Included in the Review.

Study Authors, Year & Location	Study Design	No. of patients / Mean age (years)	Intervention	Outcome	Outcome Measure	Findings
Capone F et al, 2017[1] Italy	RCT	N=42 - RG=21 -SG=21 Mean age -RG= 53.7 ± 15.6 -SG= 55.6 ± 15.9	RG = robot assisted therapy +ta- VNS SG = robot assisted therapy +sham ta-VNS -For 10 consecutive working days	-Stroke related neurological deficit - Level of spasticity -Degree of disability and dependence in doing ADLs -Level of assistance required -UE functional motor impairment	-National Institute of Health Stroke Scale -Rankin Scale -Barthel Index -Modified Ashworth Scale - FMA UE	Both real and sham patients improved after the intervention but the change in FM was significantly higher for the real group.

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Redgrave JN et al, 2018[10] United Kingdom	PRCT	N= 13 -EG=7 -CG=6 Mean age -64.5±6.9	EG= ta-VNS+ TOT CG= TOT only. Three times /week for 6 weeks	-UE functional motor impairment -Functional status of UE in hemiplegic -Degree of disability and dependence in doing ADLs -Level of assistance required -Psychological aspect of life after stroke -Severity of depression -Generalized anxiety -Level of chronic Fatigue	- FMA UE -action Recovery Arm Test -Modified Rankin score -Barthel Index -Stroke Impact Scale -Motor Activity Log Patient Health Questionnaire -Generalised Anxiety disorder 7 -Fatigue Assessment Scale	There was a significant change in the UFM, ARAT, SIS, FAS score after following the mentioned protocol
Wu D et al, 2020[7] China	RCT	N= 21 -RG=10 -SG=11 Mean age -RG= 64.50±9.97 -SG= 61.82±10.63	RG= conventional rehabilitation therapy +ta- VNS SG= conventional rehabilitation the-rapy +sham ta- VNS For 15 consecutive days for 4 weeks	-UE functional motor impairment -UE motor ability -Patient's functional independence in performing activity -Level of spasticity and flaccidity	-Wolf Motor Function Test - FMA UE -Functional Independence Measurement -Upper Limb Brunnstrome Stage	FMA-U, WMFT, and FIM scores were significantly higher in ta- VNS group compared with sham-ta- VNS group
Chang JL et al, 2021[2] United States	RCT	N= 36 -RG-18 -SG-18 Mean age -59.02 ± 1.98	RG = shoulder/ elbow robotic therapy paired with active ta- VNS SG = shoulder/elbow robotic therapy paired with sham ta-VNS 9 sessions (3x/week for 3 weeks)	-Upper extremity (UE) functional motor impairment -UE motor abilities -Quantify spasticity	-UE FMA -Medical Research Council Motor Power Scale -Wolf Motor Function Test -Modified Tardieu Scale	There were significant motor improvements after robotic training for both sham and active ta-VNS groups, and these improvements were enhanced at follow-up
Bardan BW et al, 2023[9] USA	PRCT	N= 20 -EG=10 -CG=10 Mean age -EG= 57.33±8.28 -CG= 58.71±6.45	EG= MAAVNS CG=active unpaired ta-VNS +12 TST 1 to 1.5 hours/session for 4 weeks.	-UE functional motor impairment -UE motor ability	-Wolf Motor Function Test - FMA UE	MAAVNS provide significant improvement to stroke survivors with motor function deficits
Wang L et al, 2023[8] China	PRCT	N= 27 -LH=15 -RH=12 Mean age -LH= 63.6±10.53 -RH= 60.58±12.42	Ta-VNS-left hemiplegia (LH)= ta-VNS + performing the block tasks ta-VNS-right hemiplegia(RH) = residual effects of the ta-VNS + performing the block task For 30 min.	-Patient's ability to perform everyday task -UE functional motor impairment -Level of assistance required	-Simplified Upper Limb Function Test - FMA UE -Modified Barthel Index	There is significant difference in motor function of both the groups than the baseline but the activation region was broader and more intense in patients with left-side hemiplegia to right-side hemiplegia
Weng MH, et al 2024[3] China	RCT	N= 42 - VNS group =21 -SG=21 Mean age -RG=55 ± 11 -SG=57 ± 11	VNS group= real ta-VNS + TOT SG= sham ta-VNS + TOT delivered 5 days per week for 4 weeks.	-UE functional motor impairment -Functional status of UE in hemiplegic -Level of assistance required	- FMA UE -Action Research Arm Test -Modified Barthel Index	The VG showed significant improvements in FMA UE, Action Research Arm Test, Modified Barthel Index and activities of daily living compared to the SG
Xiao XZ et al, 2024[4] China	RCT	N= 150 50 each Mean age -59.1±10.2 - 61.1± 9.2	three groups: concurrent ta-VNS, sequential ta-VNS, or sham control condition. Each participant will receive 14 treatment sessions on a daily basis for 14 days.	-UE functional motor impairment -Upper limb function assessment	- FMA -Upper Limb Function Assessment	Upper limb motor function was significantly enhanced in concurrent group compared to the other two groups, as indicated by the FMA-UE scores
Liping et al, 2024[5] China	RCT	N= 42 -RG=21 -SG=21 Mean age -RG= 53.7 ± 15.6 -SG= 55.6 ± 15.9	RG= ta-VNS + Rehabilitation training SG= sham Ta-VNS + Rehabilitation training 30 min per time, 5 times per week for 3 weeks	-UE functional motor impairment - UE motor abilities - Patient's functional independence in performing activity	- FMA-UE - Wolf Motor Function Test - Functional Independence Measurement	The ta-VNS showed significant improve-ments in upper extremity function, and improved tendency of per-forming daily living activities compared to the sham group

Li JN et al, 2025[6] China	RCT	N= 60 - ta-VNS group =30 -CG=30 Mean age- ta-VNS group = 69.2±12.3 -CG= 68.3±12.1	ta-VNS group = ta-VNS +conventional rehabilitation therapy CG=only conventional rehabilitation therapy periodically during the first year.	-UE motor ability -functional motor impairment -psychological aspect of life after stroke -anxiety and depression in patient	-Wolf Motor Function Test - FMA -Stroke Impact Scale -Hospital Anxiety and Depression Scale	The improvements in WMFT (time and score), FMA-U, FMA-L, and FMA-S in the ta-VNS group were significantly higher than those in the control group

RCT- Randomised Control Trial, RG- Real Group, SG- Sham Group EG- Experimental group, CG- Control Group, FMA-UE- Fugl Meyer Assessment-upper extremity, PRCT- Pilot randomised control study

CONCLUSION

In this review, t-VNS combined with other rehabilitation interventions was found effective in improving upper limb motor function, reduce spasticity, degree of disability and dependence in doing ADLs, reduce level of assistance required, decrease severity of depression and anxiety, improved chronic fatigue. There were no significant adverse effect reported in the included trials. In view of the findings of this review , it can be recommended that t-VNS can be integrated in the main line of treatment of stroke patients with upper limb dysfunction. However, the studies were limited by small sample size, lack of long-term follow-up, and unclear mechanisms behind the observed improvements. More diverse stroke population, and comparisons with other rehabilitation methods are needed for more definitive conclusions. Studies with larger sample size and longer follow up need to be conducted to enhance the generalizability of the results and to evaluate long term effects of t-VNS in patients with stroke. The review underlines the role of non-invasive vagus nerve stimulation for upper limb rehabilitation in stroke patients. Thus, this technique can be integrated in the main line of treatment to improve outcomes in patient with stroke.

Declarations

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Conflict of Interest: The authors report no conflict of interest
Ethical Approval: Not required

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