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Research Article

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The Influence of Magnetic Resonance Imaging and Adjunct Acupuncture on Long-Term Pain Improvement for Patients with Trigeminal Neuralgia

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Abstract

Trigeminal neuralgia is a debilitating disease characterized by neuropathic facial pain which significantly impact on the patient's quality of life and socioeconomic function. For patients with trigeminal neuralgia, Magnetic Resonance Imaging (MRI) is a routine investigation recommended in recent clinical guidelines but it remains unclear whether its use has any impact on patient-reported clinical outcomes. Acupuncture as an adjunct therapy has been shown to provide short term pain relief but its longer-term benefits remain unknown. The aims of the study are to examine whether the use of MRI and/or adjunct acupuncture is associated with the long-term pain improvement for trigeminal neuralgia patients, and thus to inform on prognosis of trigeminal neuralgia.

***Methods:** In this retrospective cohort study using data from routine clinical practice, we included all adult patients diagnosed with trigeminal neuralgia and managed at the Pain Management Centre, Singapore General Hospital between 2011 and 2017. Patients who have incomplete clinical data or lost to follow up are excluded. Logistic regression model was used to examine the association between the uses of MRI or adjunct MRI and pain symptom improvement at 6-12 months follow up.*

***Results:** Fifty-three patients were identified and included in this study. Neither the use of MRI nor acupuncture was found to be significantly associated with pain improvement for patients with trigeminal neuralgia at 6 to 12 months follow up after the initial diagnosis.*

***Conclusion:** The use of MRI or adjunct acupuncture did not seem to be related to long-term pain improvement for patients with trigeminal neuralgia and thus has limited prognostic value. These findings would have to be confirmed by further studies of larger sample size, and ideally with prospective randomized clinical trials.*

Keywords: Trigeminal Neuralgia, Magnetic Resonance Imaging, Acupuncture, Pain

Introduction

Trigeminal neuralgia (TN) is a debilitating disease characterized by episodic, unilateral, electric shock-like neuropathic facial pain that is touch-evoked in one or more divisions of the trigeminal nerve [1-3]. It has significant impact on the quality of life and the socioeconomic functioning of the patients [4-9]. Although it is well known that trigeminal neuralgia is associated with vascular compression of the trigeminal nerve root and that demyelination of trigeminal nerve is the predominant disease mechanism, the exact pathophysiology and etiological factors of the disease remain speculative [1,3,7]. Magnetic resonance imaging (MRI) is recently recommended in the 2019 European Academy of Neurology guideline on trigeminal neuralgia as a part of early work up in patients with characteristic symptoms of facial pain and/or sensory deficits and can also be used for classification purposes by helping to distinguish between idiopathic trigeminal neuralgia (no neurovascular contact or neurovascular contact without morphological changes of the

trigeminal root), classical TN (due to neurovascular compression with morphological changes of the trigeminal root), and secondary TN (due to major neurological disease such as cerebellopontine angle tumors or multiple sclerosis) [2-8]. However, it remains unclear whether the use of MRI would improve management and hence clinical outcomes of patients with trigeminal neuralgia. To the best of our knowledge, there is no prior study on the use of MRI and its impact on patient-reported outcomes in trigeminal neuralgia patients.

Long-term treatment of trigeminal neuralgia includes medical, surgical, and adjunct options. Carbamazepine is considered the gold-standard for the initial medical treatment for trigeminal neuralgia although oxcarbazepine, lamotrigine, gabapentin, botulinum toxin type A, baclofen and phenytoin have also been used in clinical practice albeit with low quality evidence [8]. Many surgical techniques have been used, including micro vascular decompression, gamma knife surgery, radiofrequency thermo coagulation, partial sensory rhizotomy, balloon decompression, and glycerol rhizolysis, but also have only low quality evidence and low to moderate efficacy [8]. Despite recent advances in therapeutics, the efficacy of mainstream medical therapies remains unsatisfactory, due to drug intolerance, decrease of therapeutic effect over time and high incidence of symptom recurrence [9, 10]. Acupuncture, a complementary medicine modality, has been demonstrated to have analgesic effects with low rates of complications. Possible mechanisms of action including suppression of nociceptive pathways and modulation of tissue perfusion and electrolytes concentrations across neuronal membranes [11-14]. In recent years, acupuncture has been increasingly used in patients with trigeminal neuralgia, which has been identified by the World Health Organization as one of the medical conditions that may be effectively treated with acupuncture [14, 15]. A randomized controlled trial showed that trigeminal neuralgia patients who received acupuncture intervention in addition to carbamazepine, compared to the control group which received carbamazepine alone, have improved cognitive function and quality of life [14]. In a recent systematic review and meta-analysis, acupuncture alone compared with carbamazepine alone showed superior clinical efficacy in terms of response rate, pain score, as well as recurrence rate while acupuncture combined with carbamazepine in contrast to carbamazepine alone demonstrated a better response rate [9]. However, the included studies were all from mainland China and the overall quality of evidence as measured using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system was deemed to be "low" or "very low" [16]. Additionally, the study duration and follow up period of most of the included studies were within one month. Hence, it is unknown whether the use of acupuncture improves pain symptoms in the longer term.

The primary aim of this study is to investigate whether the use of MRI or adjunct acupuncture is associated with pain improvement in patients with trigeminal neuralgia at 6 to 12 months follow up after the initial diagnosis (taken as the first visit to the Singapore General Hospital Pain Management Centre).

Materials and Methods:

Participants

All adult patients diagnosed with trigeminal neuralgia and managed at the Pain Management Centre, Singapore General Hospital between 2011 and 2017 were included. Patients who defaulted follow up or who had incomplete clinical data were excluded.

Data extraction

Deidentified clinical records and MRI findings of the study participants were retrieved. Data extracted include age at first clinic visit, gender, race, side of pain in the face, number of cranial nerve V divisions involved, severity of baseline pain (mild, moderate, severe), number of medications at diagnosis, adjunct acupuncture use, severity of pain at 6-12 months follow up, availability of MRI brain reports at diagnosis or during follow up, number of clinic visits within 1 year. This study was approved by Sing Health Centralized Institutional Review Board (CIRB Ref: 2018/2292).

Statistical Analysis

We first conducted a unilabiate analysis between the groups of patients with acupuncture use vs no acupuncture use. This is followed by unilabiate logistic regression with the outcome of interest being pain improvement at 6-12 months follow up (improved vs not improved). Finally, we carried out multivariable logistic regression with the outcome of interest being pain improvement at 6-12 months follow up (improved vs not improved), adjusted for significant confounders (if $p<0.2$ in the unilabiate logistic regression model).

Results

Patient's profiles

Sixty-two patients were initially screened and 53 patients were included in this study (nine patients were excluded as they had other diagnoses than TN). Table I shows their baseline demographics, clinical characteristics, and pain improvement at 6-12 months follow up. In the overall study population, majority of the patients are above 60 years old and of Chinese ethnicity with right sided facial pain that is of mild to moderate severity at baseline.

Table I: Baseline characteristics of study population

		Study Population	Acupuncture			
Baseline Characteristics		**N=53**	**No N=32**	**Yes N=21**	**Parametric P-value***	**Non-Parametric P-value****
Age at first visit	Mean (SD)	62.34 (13.01)	63.75 (13.20)	60.19 (12.73)	0.335	0.283
Gender	Female N (%)	32 (60.4)	16 (50)	16 (76.2)	0.057	0.085
	Male N (%)	21 (39.6)	16 (50)	5 (23.8)		
Race	Chinese N (%)	43 (81.1)	24 (75)	19 (90.5)	0.159	0.282
	Non-Chinese N (%)	10 (18.9)	8 (25)	2 (9.5)		
Side of pain	Left N (%)	19 (35.8)	12 (37.5)	7 (33.3)	0.757	1.000
	Right N (%)	34 (64.2)	20 (62.5)	14 (66.7)		
Severity of baseline pain	Mild N (%)	22 (41.5)	13 (40.6)	9 (42.9)	0.968	1.000
	Moderate N (%)	20 (37.7)	12 (37.5)	20 (37.7)		
	Severe N (%)	11 (20.8)	7 (21.9)	4 (19.0)		
MRI available	No N (%)	21 (39.6)	14 (43.8)	7 (33.3)	0.448	0.569
	Yes N (%)	32 (60.4)	18 (56.2)	14 (66.7)		
Number of CN V divisions involve	Mean (SD)	1.57 (0.50)	1.56 (0.50)	1.57 (0.51)	0.950	0.949
Number of medications at diagnosis	Mean (SD)	1.98 (0.84)	2.03 (0.90)	1.90 (0.77)	0.598	0.595
No of visits within 1yr	Mean (SD)	4.94 (2.09)	4.97 (1.99)	4.9 (2.28)	0.914	0.536
Pain improvement at 6-12mths	Improved N (%)	39 (74)	24 (75)	15 (71.4)	0.773	1.000
	Not improved N (%)	14 (26)	8 (25)	6 (28.6)		

Comparing the patients with acupuncture use vs those without acupuncture use, the difference between the baseline variables is not statistically significant.

Association between the use of adjunct acupuncture or MRI and pain score improvement

As shown in Table II, in the unilabiate logistic regression model with outcome being pain improvement at 6-12 months follow up (Yes or No), no variable has demonstrated a statistically significant association with the outcome. In the multivariable logistic regression model using the same outcome and adjusted for the severity of baseline pain (Table III), neither the use of acupuncture (Adjusted Odds Ratio (95% confidence interval) 0.83 (0.23, 2.97), p value 0.7726) nor the availability of MRI (Adjusted Odds Ratio (95% confidence interval) 0.80 (0.22, 2.93), p value 0.7393) has significant association with pain improvement at 6-12 months follow up.

Table II: Univariate logistic regression for pain improvement at 6-12 month (yes vs no)

Variable	Event vs Reference Level	Un-Adjusted Odds Ratio (95% CI)	P value	Omnibus P value
Age at first visit		1.01 (0.97, 1.06)	0.5659	
Gender	M vs F	0.83 (0.24, 2.82)	0.7621	
Race	Chi vs Non-Chi	0.74 (0.15, 3.75)	0.7171	
Acupuncture use	Yes vs No	0.83 (0.24, 2.82)	0.7621	
Side of pain	Left vs Right	0.45 (0.13, 1.57)	0.2120	
Severity of pain at baseline	Moderate vs Mild	5.21 (1.05, 25.7)	0.0825	0.1283
	Severe vs Mild	1.71 (0.36, 8.07)	0.7104	
MRI availability	Yes vs No	0.82 (0.24, 2.88)	0.7625	
Number of CN V divisions involved		0.98 (0.29, 3.33)	0.9783	

Number of medications		1.67 (0.76, 3.68)	0.2010	
Number of visits within one year		1.04 (0.77, 1.40)	0.8009	

Table III: Multivariable logistic regression for pain improvement at 6-12 month (yes vs no)

Variable	Event vs Reference Level	Adjusted Odds Ratio* (95% CI)	P value	Omnibus P value
Age at first visit		1.02 (0.97, 1.07)	0.4942	
Gender	M vs F	0.73 (0.20, 2.64)	0.6304	
Race	Chi vs Non-Chi	0.61 (0.11, 3.26)	0.5620	
Acupuncture use	Yes vs No	0.83 (0.23, 2.97)	0.7726	
Side of pain	Left vs Right	0.57 (0.16, 2.06)	0.3900	
Severity of pain at baseline	Moderate vs Mild	5.21 (1.05, 25.7)	0.0825	0.1283
	Severe vs Mild	1.71 (0.36, 8.07)	0.7104	
MRI availability	Yes vs No	0.80 (0.22, 2.93)	0.7393	
Number of CN V divisions involved		1.03 (0.29, 3.66)	0.9628	
Number of medication		1.62 (0.73, 3.60)	0.2371	
Number of visits within one year		0.88 (0.63, 1.24)	0.4775	

* Adjusted for Severity of baseline pain

Discussion

Our study shows that neither the use of MRI nor acupuncture is significantly associated with pain improvement in patients with trigeminal neuralgia at 6 to 12 months follow up after the initial diagnosis. Our study, to the best of our knowledge, is the first study that examines the use of MRI and its impact on patient-reported clinical outcomes in patients with trigeminal neuralgia. It also builds on the growing evidence supporting the use of acupuncture as an adjunct in pain management by assessing its long-term therapeutic effects in our population with trigeminal neuralgia.

The current recommendation of using MRI as a routine part of early work up for patients with trigeminal neuralgia is largely focused on classification and investigation of disease etiology from an anatomical perspective [2]. MRI is undoubtedly helpful to exclude secondary causes of pain such as tumors or multiple sclerosis as clinical history and physical examination alone cannot reliably rule these out [3]. There is however, no prior study examining whether the MRI findings translate to changes in management and hence clinical outcomes, particularly, patient-reported pain improvement. Very often, patients judge the effectiveness of medical interventions based on the degree of impact on their quality of life which includes frequency and severity symptoms, psychosocial stress, and functional impairment [17]. Hence, a potentially important implication of this study's findings is to aid clinicians' discussions with their patients regarding the usefulness of MRI especially as the scans can be a significant financial burden to patients. This will help facilitate the shared decision-making process between clinicians and patients regarding the efficacy of MRI.

The body of evidence regarding the use of acupuncture in pain management has been growing in recent years, especially as an adjunct in labor analgesia [18, 19] rheumatologic and orthopedic diseases [20-22]. However, the studies on the use of acupuncture for patients with trigeminal neuralgia have failed to draw a robust conclusion regarding the efficacy of acupuncture, as reflected by a recent systematic review and meta-analysis [9]. The studies included in the meta-analysis were limited by their short follow up periods, lack of standardization of acupuncture points and acupuncture manipulation techniques (e.g. deep vs superficial needling, needle retention time), and demonstrating insufficient methodological rigour. The recently proposed consolidated standards of reporting trials (CONSORT) for traditional Chinese medicine may provide opportunities for high quality trials on acupuncture in the future [23]. Our study builds on the previous findings by assessing patients over a longer follow up period. Further studies may examine the risk factors affecting poor treatment outcome of TN, including psychological risk factors, as well as the etiology of TN, which allows for individualized treatment and prognostication for these patients.

An important limitation of our study is its small sample size. This prevents definitive conclusion of the negative results of this study due to insufficient power. Another limitation is that the patients included in this study are from a single center. The generalizability and applicability to other patient populations may be limited.

In conclusion, the use of MRI or adjunct acupuncture may not help with pain improvement in the long-term for patients with trigeminal neuralgia. Future studies of larger sample size and multiple centers are needed to confirm the results of this study.

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