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CLINICAL TRIAL REPORT

The Effect of Gua Sha Therapy on Pain in Parkinson's Disease: a Randomized Controlled Trial

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Purpose: Pain is a common yet undertreated symptom of Parkinson's disease (PD). This study investigated the effect of Gua Sha therapy on pain in patients with PD.

Patients and Methods: A total of 56 PD patients with pain were randomized into either the experimental group (n=28), receiving 12 sessions of Gua Sha therapy, or the control group (n=28) without additional treatment. Participants underwent assessment at baseline, after the twelfth invention, and at the 2-month follow-up timepoints. The primary outcome was KPPS and VAS. Secondary outcomes included UPDRS I–III, PDSS-2, HADS, PDQ-39, and blood biomarkers (5-HT, IL-8, IL-10).

Results: The experimental group reported a significant improvement in pain severity, motor functions, affective disorder, and sleep quality ($P < 0.05$). Furthermore, increasing trends in both 5-HT and IL-10, as well as decreasing trends in IL-8 were observed. No serious adverse events occurred.

Conclusion: The preliminary findings suggest that Gua Sha therapy may be effective and safe for alleviating pain and improving other disease-related symptoms in PD patients.

Keywords: Parkinson's disease, pain, Gua Sha therapy, randomized controlled trial

Introduction

Parkinson's disease (PD) is a common, chronic, and progressive neurodegenerative disease. Although the clinical feature of PD is dominated by typical motor symptoms, patients also suffer from various non-motor symptoms (NMS), which often occur throughout PD and have a more significant impact.[1,2]

Pain is one of the most frequent and troublesome NMS in PD, affecting approximately 40% to 85% of the patients.[3] Pain is an independent predictor of reduced quality of life.[4] Research has shown that pain is correlated most strongly with sleep disorder, impairing sleep quality and sleep structure, and negatively interacts with depression and cardiovascular disturbance.[5–7] The pathophysiology underlying pain in PD is complex and not fully understood. Research suggests that dysfunctions in the basal ganglia circuit and monoaminergic pathways,[8,9] as well as neural inflammation, may contribute to the pain in PD.[10] These abnormalities can impair descending pain modulation, heightening pain perception and transmission. Additionally, pain in PD can also result from rigidity, akinesia, postural abnormalities, and motor complications.[11]

Despite the high prevalence and significant impact, it's a symptom that is under-recognized and inadequately treated. However, there is limited literature to date exploring interventions for pain management in PD. Most interventions, including dopamine agonists, opioids, duloxetine, and non-drug therapies, have demonstrated inadequate relief and require further investigation.[12–14] Therefore, it's necessary to explore more promising interventions to relieve pain in PD and develop additional options for both patients and healthcare professionals.

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Gua Sha therapy is one of the most commonly used non-pharmaceutical treatments in Chinese traditional medicine, based on the theory of meridians and acupoints.[15] It is an external technique that uses a smooth-edged instrument to press-stroking on treatment areas of the body creating intentionally transient petechiae and ecchymosis.[16] Gua Sha is low-cost and generally well-accepted, with little or no discomfort. These therapeutic petechiae and ecchymosis typically fade within 3–5 days.[17] Gua Sha has long been used clinically for pain relief.[16,18–20] Research suggests that its analgesia effect may result from a cascade of physiological interactions between the nervous system and the immune system.[20,21] Gua Sha can attenuate inflammatory cytokines, increase anti-inflammatory factors, elevate NO levels, and inhibit the neuronal response triggered by the activation of microglial cells, leading to antinociception and neuromodulation effects.[17,22]

In this context, we proposed the hypothesis that Gua Sha therapy can relieve PD-related pain. The aim of this study is to investigate the effect of Gua Sha therapy and its potential mechanisms in relieving pain in PD.

Materials and Methods

Study Design

This prospective, single-blinded, randomized controlled clinical trial aimed to assess the feasibility and effectiveness of Gua Sha therapy in alleviating pain with PD. Eligible patients were randomly allocated to either the experimental group or control group. A study coordinator, who was not involved in subsequent tasks, employed an automated randomization system (www.randomizer.org) to generate the random sequence. The randomization numbers were enclosed in sealed opaque envelopes, each containing the corresponding group assignments. Randomization took place immediately following baseline assessment for each patient. After the inclusion of each patient, the researcher opened the next envelope to reveal their group assignment. The data analyst remained blinded to group assignment, assessment and treatments throughout the study.

Participants

Patients with PD experiencing pain were recruited from Changshu Hospital of Traditional Chinese Medicine (Suzhou, China) between December 2022 and October 2023.

Inclusion criteria were: 35–75 years old; diagnosis of PD (according to the UK Brain Network criteria) confirmed by an experienced neurologist; Hoehn and Yahr stage 1–3; Mini-Mental State Examination (MMSE) score>24; Visual Analogue Scale (VAS)>3 for at least three month; stable anti-Parkinson's medication treatment. Exclusion criteria were: history of Deep Brain Stimulation surgery; presence of unpredictable drug fluctuations and severe motor complications; diagnosis of conditions causing pain unrelated to PD, such as fibromyalgia, radiculopathy, inflammation, or neuropathy; presence of medical contraindications with Gua Sha, such as coagulation disorders or skin injury in the treatment area.

The experimental procedures were approved by the Ethics Committee of the Changshu Hospital of Traditional Chinese Medicine (approval number: 202202043), and registered at Clinical Trials.gov on December 1, 2022 (Identifier: ChiCTR2200066343). The study complies with the Declaration of Helsinki. All participants provided written informed consent before being included.

Sample Size

The sample size was calculated through the formula: $n_1=n_2=2[(Z_\alpha+Z_\beta)\sigma/\delta]^2$, based on a power of 0.10, α error probability of 0.05, from a previous study,[23] the estimated total sample size was 60 cases.

Intervention

All participants received conventional anti-Parkinson's disease medication treatment. Patients in the experimental group underwent twelve sessions of Gua Sha therapy, once a week, for three months.

Treatment areas include the head, the back, and the painful areas such as the upper limbs, lower legs, and feet. Wearing disposable medical gloves, the researchers applied a smooth-edged instrument to patients' skin in downward strokes (Figure 1). Press strokes were repeated in one location until the appearance of petechiae (Sha), and the pressure

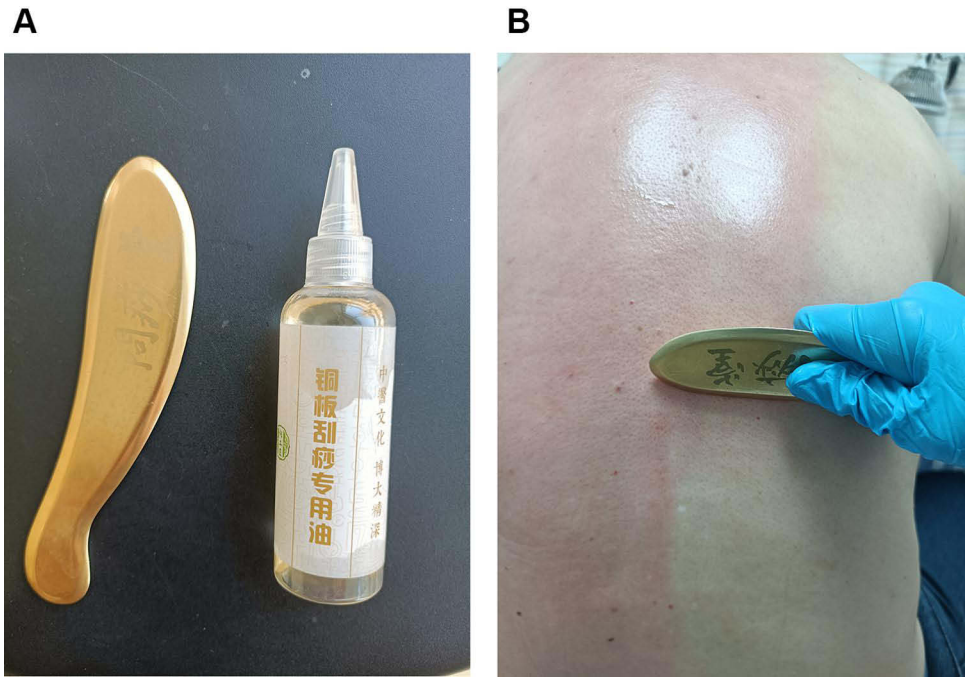

Figure 1 (A) Instruments used for Gua Sha therapy in the study. **(B)** Press-strokes were repeated in one location until appearance of petechiae.

applied was adjusted to patients comfort. Individual treatment typically lasted 40 minutes. After treatment, patients were advised to rest briefly, drink warm water, and then leave.

When scraping the head, they initiated the process by scraping the Baihui (GV20). Using Baihui (GV20) as the center, they scraped outward in a radiating motion towards the hairline, focusing on Sishencong (EX-HN1), Shenting (GV24), Yintang (GV29), Fengchi (GB20), and Fengfu (GV16). For the back, patients' backs were first covered with soothing lotion (main ingredients: mineral oil, grapeseed oil, and Artemisia argyi oil). The practitioners then scraped from top to bottom, starting with the Du Meridians, followed by the Jiaji points (EX-B2), and the Bladder Meridian of the Foot Taiyang on the back. Finally, scraping the painful areas according to the patient's pain condition. When the meridians become congested or lose vitality, they may become depleted and lack the nourishment necessary for proper function. This can lead to qi and blood stasis, which may result in pain. By activating these meridians, the circulation of qi and blood can be improved, thus alleviating pain.

Outcomes

The participants underwent assessments at baseline (T0), at the end of the twelfth intervention (T1), and during a 2-month follow-up period (T2). The researcher, who undertook assessments, employed various measures to assess the outcomes of the study comprehensively. The primary outcome was on pain intensity measured through the King's Parkinson's Disease Pain Scale (KPPS) and Visual Analogue Scale (VAS). Non-motor symptoms were evaluated using the Unified Parkinson's Disease Rating Scale I (UPDRS I), daily activities were assessed with UPDRS II and motor symptoms with UPDRS III. Sleep quality was examined using the Parkinson's Disease Sleep Scale-2 (PDSS-2), and affective disorders were established through the Hospital Anxiety and Depression Scale (HADS). The 39-item Parkinson's Disease Questionnaire (PDQ-39) was employed to assess the quality of daily life activities.

In addition to clinical assessment, blood biomarkers, including 5-Hydroxytryptamine (5-HT), Interleukin-8 (IL-8), and Interleukin-10 (IL-10), were also evaluated to understand biochemical changes between the two groups. Before treatment and at 3 months post-treatment (immediately after the 12th Gua Sha session), 1 mL of venous blood was collected from the patients. The blood samples were allowed to stand at room temperature for 30 minutes and then centrifuged at 3000 rpm for 10 minutes (with a centrifugation radius of 18.5 cm) to obtain serum. All serum samples

were kept at −80°C until testing. The levels of serum 5-HT, IL-8, and IL-10 were detected using enzyme-linked immunosorbent assay (ELISA). The reagent kits were provided by Shanghai Sai Fei Biotechnology Co., Ltd.

Safety

The treatments were administered by two experienced researchers, who received expert training and passed the examination of Gua Sha therapy. During the treatment, researchers closely monitor the patients' feedback. All patients were asked to report any adverse events during the study.

Statistical Analysis

The statistical analysis was performed using IBM SPSS 25.0 software. Baseline characteristics were presented as standard deviation (SD) or median (quartile). The independent *t*-test or X^2-square test was applied to compare the homogeneity between the two groups. The Generalized Estimating Equations (GEE) model was used to analyze the VAS, KPPS, UPDRS I–III, PDSS-2, HADS, and PDQ-39 scores for both groups at T0, T1, and T2. Independent *t*-tests were conducted to compare the changes in 5-HT, IL-8, and IL-10 between the two groups. Statistical significance was set at $P<0.05$.

Results

Patients' Characteristics

A total of 86 patients were screened for eligibility, of whom 56 were enrolled and randomized into either the experimental group (n=28) or the control group (n=28). Figure 2 presents the flow of the study. The mean age of all patients was 66.9 years (SD=9.0). The majority of them were female (54%). The average duration of PD was 7.4 years (SD=4.4), and the average duration of pain was 4.5 years (SD=3.0). The most common pain locations were the lower back, shoulders, upper back, and neck. No significant between-group differences in demographics and clinical characteristics (Table 1).

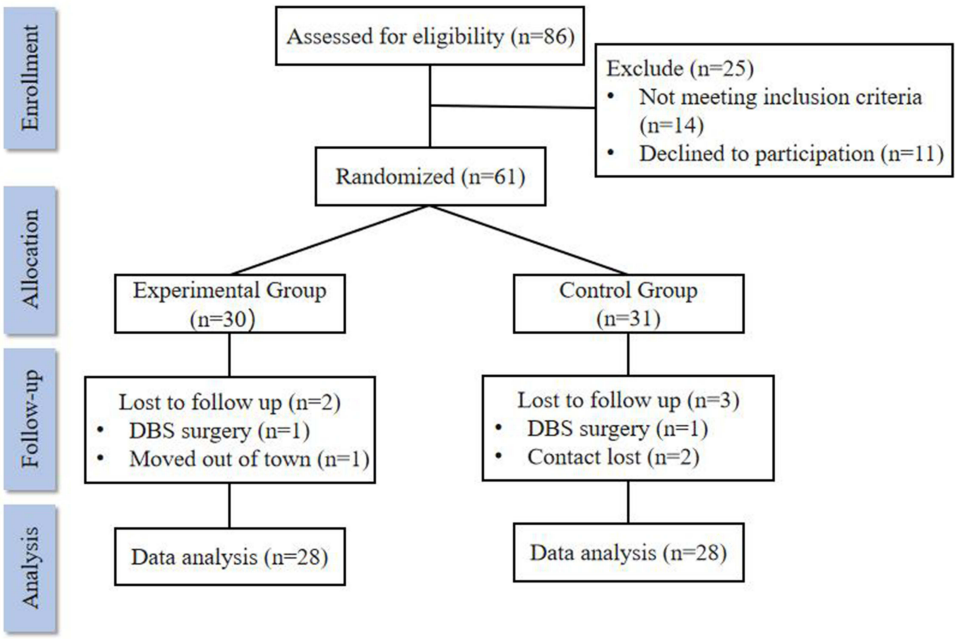

Figure 2 Flowchart of the study.

Table 1 Demographic and Clinical Characteristics of Participants

Characteristic	EG (n=28)	CG (n=28)	t/X^2	*P*
Age	65.29±10.91	68.57±6.33	−1.378	0.175
Gender (female/male)	10/18	16/12	2.585	0.108
BMI	23.19±3.39	22.63±3.48	0.609	0.545
Disease duration	6.82±4.07	7.93±4.80	−0.87	0.388
H-Y stage	2.00(1.50,2.50)	2.50(1.63,2.88)	−1.692	0.091
Pain duration	3.00(2.00,7.50)	3.00(3.00,6.50)	−0.577	0.564
VAS	6.00(5.30,7.00)	6.00(5.00,6.75)	0.203	0.840
KPPS	22.50(15.25,26.75)	22.00(16.50,25.00)	−0.430	0.669
UPDRS I	12.50(9.25,15.75)	13.00(10.25,17.75)	1.078	0.286
UPDRS II	12.00(10.00,13.75)	13.00(10.00,17.25)	1.421	0.161
UPDRS III	25.50(14.25,33.00)	28.00(22.00,37.25)	1.921	0.060
PDSS-2	23.00(18.00,30.75)	23.50(17.25,28.75)	0.159	0.874
HADS-A	6.50(3.00,8.00)	7.00(6.00,8.75)	−1.710	0.093
HADS-D	6.00(4.00,8.75)	6.50(5.00,9.00)	−1.708	0.093
PDQ-39	25.50(19.00,34.25)	32.00(26.00,36.75)	1.907	0.062

Abbreviations: BMI, Body Mass Index; VAS, Visual Analogue Scale; KPPS, King's Parkinson's Disease Pain Scale; UPDRS, Unified Parkinson Disease Rating Scale; PDSS-2, Parkinson's Disease Sleep Scale-2; HADS, Hospital Anxiety and Depression Scale; PDQ-39, the 39-item Parkinson's Disease Questionnaire.

Primary Outcomes

Table 2 presents the primary and secondary results. The VAS and KPPS scores of the Gua Sha group were significantly lower than those of the control group at both the T1 and T2 stages, demonstrating a statistically significant difference ($P < 0.001$).

Table 2 Clinical Effectiveness of Gua Sha Therapy in PD with Pain

Outcome	EG(n=28)	CG(n=28)	Adjusted Mean Difference (95% CI)	*P*-value
VSA				
T0	6.00(5.30,7.00)	6.00(5.00,6.75)	−0.07(−0.75,0.60)	0.836
T1	3.50(2.00,4.00)	6.00(5.00,7.00)	−2.54(−3.16,-1.91)	<0.001
T2	4.00(2.25,5.00)	6.00(6.00,7.00)	−2.32(−3.14,-1.51)	<0.001
KPPS				
T0	22.50(15.25,26.75)	22.00(16.50,25.00)	0.96(−3.36,5.28)	0.662
T1	10.00(7.00,15.75)	23.00(17.00,25.75)	−10.93(−14.56,-7.29)	<0.001
T2	13.50(9.00,18.00)	25.00(20.25,28.00)	−11.32(−15.48,-7.16)	<0.001
UPDRS I				
T0	12.50(9.25,15.75)	13.00(10.25,17.75)	−1.25(−3.48,0.98)	0.272
T1	7.00(5.00,10.75)	15.00(11.25,18.00)	−6.61(−8.51,-4.07)	<0.001
T2	10.00(6.00,13.00)	16.00(14.25,19.75)	−6.68(−8.63,-4.73)	<0.001
UPDRS II				
T0	12.00(10.00,13.75)	13.00(10.00,17.25)	−1.57(−3.70,0.56)	0.148
T1	8.00(5.25,10.75)	14.50(11.00,18.00)	−6.89(−9.30,-4.48)	<0.001
T2	9.50(6.25,11.00)	15.00(12.25,20.00)	−7.29(−9.73,-4.84)	<0.001
UPDRS III				
T0	25.50(14.25,33.00)	28.00(22.00,37.25)	−5.36(−11.16,0.44)	0.07
T1	18.50(10.25,26.75)	30.00(24.50,43.00)	−14.46(−19.91,-9.01)	<0.001
T2	22.00(12.50,25.75)	35.00(24.75,43.00)	−13.64(−18.66,-8.62)	<0.001

(*Continued*)

Table 2 (Continued).

Outcome	EG(n=28)	CG(n=28)	Adjusted Mean Difference (95% CI)	*P*-value
PDSS-2				
T0	23.00(18.00,30.75)	23.50(17.25,28.75)	−0.32(−4.22,3.57)	0.871
T1	13.00(11.00,16.75)	21.00(19.00,28.50)	−8.93(−12.07,-5.79)	<0.001
T2	15.00(11.25,20.75)	24.00(22.00,28.50)	−8.93(−12.33,-5.52)	<0.001
HADS-A				
T0	6.50(3.00,8.00)	7.00(6.00,8.75)	−1.21(−2.58,0.15)	0.082
T1	4.00(1.25,6.00)	8.00(6.00,10.00)	−3.79(−5.13,-2.44)	<0.001
T2	5.00(2.25,8.00)	8.00(6.25,10.75)	−3.64(−5.13,-2.16)	<0.001
HADS-D				
T0	6.00(4.00,8.75)	6.50(5.00,9.00)	−1.32(−2.81,0.17)	0.082
T1	3.00(1.00,4.75)	7.00(6.00,9.75)	−4.79(−5.99,-3.58)	<0.001
T2	5.00(2.25,6.00)	9.00(7.00,11.00)	−4.39(−5.62,-3.17)	<0.001
PDQ-39				
T0	25.50(19.00,34.25)	32.00(26.00,36.75)	−3.89(−9.13,1.35)	0.145
T1	18.50(10.75,25.50)	34.00(28.25,39.00)	−14.71(−19.39,-10.04)	<0.001
T2	21.50(13.50,30.50)	38.00(32.25,45.75)	−14.89(−20.17,-9.61)	<0.001

Abbreviations: T0, baseline; T1, immediately post-intervention; T2, two months after the intervention.

Secondary Outcomes

The experimental group showed significant improvement in UPDRS I–III, PDSS-2, HADS, and PDQ-39 scores ($P < 0.01$). At the T2 stage, the scores in the Gua Sha group increased but remained lower than before the intervention, with statistical significance ($P < 0.01$) (Appendix 1). After intervention, the levels of serum 5-HT and IL-10 in the Gua Sha group were higher than those in the control group, while the level of IL-8 was lower than that in the control group (Table 3), and the differences were statistically significant ($P < 0.01$). No adverse events were reported throughout the intervention.

Table 3 The Effect of Gua Sha Therapy on Biomarkers (ρ/Pg·mL-1)

Variable	Group	T0	T1	*Z*	*P*-value
5-HT	EG (n=28)	218.05±43.09	373.65±95.94	−8.313	<0.001
	CG (n=28)	204.60±67.81	297.25±67.23	−4.722	<0.001
	t	0.886	3.451		
	P-value	0.379	0.001		
IL-10	EG (n=28)	80.98(65.11, 87.42)	144.23(92.22, 184.53)	−4.235	<0.001
	CG (n=28)	85.72(73.61, 97.49)	86.35(69.43, 101.33)	−0.106	0.916
	Z	−1.524	−3.802		
	P-value	0.128	<0.001		
IL=8	EG (n=28)	144.10(129.18, 160.79)	87.28(86.46, 87.20)	−4.623	<0.001
	CG (n=28)	147.62(91.54, 196.58)	132.50(116.92, 120.28)	−0.797	0.425
	Z	−0.131	−6.408		
	P-value	0.896	<0.001		

Abbreviations: T0, baseline; T1, immediately post-intervention.

Discussion

This study suggests that Gua Sha therapy may be effective and safe for pain symptom, sleep quality, affective disorder, motor functions, and the quality of life in PD patients experiencing pain. Moreover, we also observed an increasing trend in 5-HT and IL-10 levels, and a decreasing trend in IL-8 levels, suggesting that Gua Sha may alleviate neuroinflammation in PD.

The mechanisms of pain in PD are multifaceted, as the disease affects structures involved in pain processing and nociceptor excitability.[24] The clinical efficacy of Gua Sha therapy in relieving PD-related pain could be attributed to several factors. Firstly, Gua Sha involves direct physical stimulation of the superficial skin and deep muscles, which may lead to muscle relaxation and joint mobility.[25] Gua Sha promotes local microcirculation while simultaneously stretching both the superficial skin and deep muscles.[26] Such effects were proposed to be linked to reducing pain levels and improving physical mobility.[27] Similar benefits have been observed in studies of Thai massage and Japanese massage,[28,29] showcasing the ability to enhance muscle flexibility, induce relaxation, and alleviate pain in PD patients.

Furthermore, exploring the physiological responses induced by Gua Sha therapy provides insight on potential mechanisms in alleviating PD-related pain. Evidence suggests that Gua Sha can modulate the interactions between the skin, nervous system, and immune system, eliciting physiological responses.[15] Research has indicated that Gua Sha therapy may enhance immune response and anti-inflammatory effects.[30] The pressure stimulation of Gua Sha on the skin leads to subcutaneous capillary rupture, with resultant blood leakage acting as a stimulus, initiating local aseptic inflammation response.[22] Our finding showed that the Gua Sha group exhibited increased plasma levels of 5-HT and IL-10, and decreased levels of IL-8 compared to the control group. Notably, serotonin is an important neurotransmitter involved in the pathophysiology of PD.[31] Previous studies have shown decreased concentrations of 5-HT in PD patients, and the lower levels of 5-HT are associated with increased pain severity.[32] IL-10, a well-known anti-inflammatory factor, also plays a significant role in PD.[33] Research[34] indicates that IL-10 suppresses microglial activation and neuronal responses, offering neuroprotective benefits and leading to pain relief.[15] In contrast, IL-8 is a pro-inflammatory cytokine implicated in inflammatory and autoimmune disorders.[35] Studies have investigated the relationship between the level of IL-8 and non-motor symptoms in PD, but the results have been inconsistent.[36,37]

Our research findings also demonstrated that Gua Sha could improve non-motors, including depression, anxiety, and sleep disorders. Pain and depression often coexist as comorbid conditions in PD,[6] and the neurobiological mechanisms underlying both may overlap to some extent.[38] Consequently, we hypothesize that Gua Sha might exert a beneficial influence on both pain and depression. Moreover, the dynamic interaction between practitioners and patients during the intervention, involving disease-related guidance and the provision of strong emotional support, contributes significantly to the therapeutic impact of Gua Sha therapy. Our findings also suggest that Gua Sha therapy improved sleep quality in PD. Gua Sha can reduce central nervous system tension and regulate humoral factors,[39] which are key factors influencing sleep patterns. Additionally, pain has a direct impact on comfort levels and the frequency of waking up during sleep. Thus, alleviating pain may be helpful to promote overall comfort and reduce disruptions in sleep.[5]

In terms of motor symptoms, patients showed significant improvements in muscle rigidity and balance disturbances. Given the limited literature on this topic, the underlying mechanisms remain unclear. When scraping the movement and sensory reflex zones in the head, it may increase cortical blood flow and stimulate the prefrontal cortex and supplementary motor area. These anatomical structures play a role in controlling balance and regulating muscle tone.[40,41] Prior research[42,43] has demonstrated that acupuncture can enhance balance function in patients with PD and stroke. Although the stimulus intensity of Gua Sha may be smaller compared to acupuncture, the broader treatment area and the longer treatment time of Gua Sha may yield similar effects. Future studies could utilize imaging technology to explore the impact of Gua Sha on the functional connectivity in the brains of PD patients with pain.

However, during the follow-up period, there was a slight increase in scale scores, suggesting the effect of Gua Sha therapy may be inconsistent. By acknowledging pain management as an ongoing, prolonged process rather than a singular intervention, the potential of Gua Sha therapy as a promising, effective, and safe treatment for PD becomes evident. However, the dose-response relationship of pain relief through Gua Sha requires long-term tracking.

There are several limitations in our study that need to be noted. Firstly, patients typically experience a combination of 2 to 3 types of pain.[4] We did not conduct a subgroup analysis based on the types of pain classification. Secondly, the assessment only included one time point (2 months) after the treatment. It is advisable to incorporate additional time points further away from the treatment to accurately measure the effectiveness of Gua Sha. Lastly, the small sample size and single-center setting of our study limit the generalizability of our findings to a large population. Further studies are recommended to recruit patients from diverse centers to enhance the reliability and applicability of the research.

Conclusion

This study conducted a preliminary exploration of the effect of Gua Sha on pain in PD. The results suggest that Gua Sha shows promise in reducing pain severity, improving depression and anxiety, enhancing sleep quality, and improving motor symptoms among PD patients. While these findings are encouraging, for further validation and extension, future research may benefit from the multi-center, large-sample studies.

Data Sharing Statement

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgement

An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified between the authors and PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

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Disclosure

The authors report no conflicts of interest in this work.

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