Am J Transl Res 2024;16(2):625-636
www.ajtr.org /ISSN:1943-8141/AJTR0151424

Original Article

Auricular acupressure combined with Tongtian oral liquid for acute attacks of migraine without aura: a single-center, retrospective study

Yuanyuan Wang[1*], Zihan Rong[2*], Pei Wang[1], Jiale Meng[3], Fei Yang[3], Ruiyi Xie[1], Zhaolu Deng[1], Sicheng Yuan[3], Tao Guo[3]

[1]Department of Nursing, Affiliated Hospital of Nanjing University of Chinese Medicine (Jiangsu Province Hospital of Chinese Medicine), Nanjing 210000, Jiangsu, China; [2]Nanjing Foreign Language School, Nanjing 210000, Jiangsu, China; [3]Department of Emergency, Affiliated Hospital of Nanjing University of Chinese Medicine (Jiangsu Province Hospital of Chinese Medicine), Nanjing 210000, Jiangsu, China. [*]Equal contributors.

Received May 25, 2023; Accepted September 7, 2023; Epub February 15, 2024; Published February 28, 2024

Abstract: Objective: To observe the effect of auricular acupressure combined with Tongtian Oral Liquid for immediate pain relief in patients with acute migraine without aura, and to analyze the risk factors that affect the number of acute attacks of migraine without aura. Methods: This retrospective study analyzed data of 180 patients diagnosed with acute migraine without aura who were admitted to Affiliated Hospital of Nanjing University of Chinese Medicine (Jiangsu Province Hospital of Chinese Medicine). The patients were divided into an intervention group 1 (n=60), an intervention group 2 (n=60), and a control group (n=60) according to different treatment methods. The intervention group 1 received auricular acupressure + Tongtian oral liquid, the intervention group 2 received Jing point bloodletting + Tongtian oral liquid, and the control group received ibuprofen + flunarizine. Before treatment, 60 minutes and 120 minutes after treatment, the visual analogue scale (VAS) and the short-form McGill pain questionnaire (SF-MPQ) were used to score the pain in the three groups to evaluate the efficacy of immediate analgesia. Symptoms including fatigue, drowsiness, nausea, and vomiting after 2 hours of treatment were observed. The amount of ibuprofen used within 24 hours was calculated. The drug treatment was continued for one month. The frequency of migraine attacks was compared among the three groups. The relevant factors affecting the number of migraine attacks were analyzed. Results: The VAS and SF-MPQ scores of the three groups were all decreased 120 minutes after treatment as compared with those before treatment (P<0.01). The decline rate in the intervention group 1 > that in intervention group 2 > that in control group (P<0.01). The immediate analgesic efficiency at 60 minutes, intervention group 1 > intervention group 2 > control group (100% vs. 76.67% vs. 56.67%, P<0.001). After 2 hours of treatment, more cases of fatigue and lethargy occurred in the control group (P<0.05). There was no significant difference in nausea and vomiting among the three groups (P>0.05). The 24-hour ibuprofen dosage and headache recurrence ratio, control group > intervention group 2 > intervention group 1 (P<0.05). The number of headache attacks within 30 days was significantly higher in the control group than in the intervention groups (P=0.012). There was no significant statistical difference between the two intervention groups (P=0.568). Regression analysis found that age (OR=1.036, 1.006-1.068), body mass index (OR=1.101, 1.008-1.201), hypertension (OR=2.879, 1.187-6.986), chronic gastritis (OR=2.839, 1.213-6.647), children with educational problems (OR=0.333, 0.164-0.676), and residual fatigue symptoms (OR=4.539, 1.828-11.271) affected the number of headache attacks within the one month of treatment. Conclusions: Auricular acupressure combined with Tongtian Oral Liquid can relieve the acute pain of migraine without aura and reduce the number of pain episodes. The curative effect of this combination is better than that of western medicine alone.

Keywords: Auricular acupressure, bloodletting at Jing points, migraine, efficacy evaluation

Introduction

Migraine is a polygenic and complex neurological disorder characterized by unilateral headache. Studies have shown that 1.25 billion people suffered from migraine in 2017 [1]. There is even more evidence that migraine has become the second leading cause of disability, more than the rest of the neurological disorders combined [2]. Migraine can be divided into

https://doi.org/10.62347/FYGE7020

migraine with aura and without based on the presence or absence of aura [3]. Migraine without aura has a wider range of incidence and a more complex pathogenesis [4]. It can cause pain and discomfort in patients. It can also use cognitive decline, organic changes in the brain, and mental illness. These greatly interfere with daily work and life [5]. Active intervention and prevention of migraine is critical in clinical settings. There is no cure for migraine, and a lack of specific medicines. The main treatment methods are analgesia in the acute phase and prevention in the remission phase. For acute analgesic treatment, western medicine uses non-steroidal anti-inflammatory drugs to relieve pain in patients. These drugs exhibit limited and short-lived analgesic efficacy, and often cause side effects. The issue of clinical overuse has emerged, prompting a search for more practical, effective, and convenient treatment methods. This pursuit has become a hot spot in clinical research. The external treatment method of traditional Chinese medicine (TCM) based on acupuncture has been proven to be able to achieve an instant analgesic effect on migraine [6]. The internal treatment method of TCM based on Tongtian Oral Liquid has been found to have a definite effect on improving migraine [7]. Experimental findings [8] have demonstrated the efficacy of auricular acupressure and Jing point bloodletting therapy in the clinical treatment of migraines. Limited research has been conducted concerning the immediate analgesic effects of these therapies, specifically for migraine without aura. This study included patients with migraine without aura in the acute stage, and observed the immediate analgesic effect of auricular acupressure on these patients.

Methods

Study design

This single-center, retrospective study included 180 patients with acute migraine without aura who were treated in the emergency center of Jiangsu Provincial Hospital of Traditional Chinese Medicine from January 2021 to October 2022. The patients were divided into an intervention group 1, an intervention group 2, and a control group by the different treatments. The intervention group 1 received auricular acupressure + Tongtian oral liquid, the intervention group 2 received Jing point bloodletting + Tongtian oral liquid, and the control group received ibuprofen + flunarizine. This study was approved by the Ethics Committee of Affiliated Hospital of Nanjing University of Chinese Medicine (Jiangsu Province Hospital of Chinese Medicine) (ethical approval number: 2021NL-174-01). This study was retrospective in nature. It did not involve the exposure of patient privacy or information. There were not any informed consent forms that needed to be signed. According to the data obtained through literature searches and clinical treatment experiences, and considering an estimated 2-hour analgesic effective rate of 65% in the control group, 95% in the intervention group 1, and 85% in the intervention group 2, with a bilateral α level of 0.05 and a power of 90%, sample size calculations were conducted using PASS 11 software. The total number of research samples in the 3 groups was determined to be 140 cases. Accounting for a 20% dropout rate, the initial sample size for the three experimental groups was set at 175 people, with 59 in each group. There was no significant difference between the three groups in terms of baseline data ($P>0.05$), indicating comparability. See **Table 1** for details.

Participants

Case selection

The diagnostic criteria for migraine without aura were according to the guidelines for the diagnosis and treatment of migraine in China (2022 edition) [9]. A. Headaches that meet criteria B-D manifest at least 5 attacks. B. Headache attacks last for 4-72 hours when untreated or poorly treated. C. To qualify as this type of headache, at least 2 of the following 4 criteria should be met: unilateral pain, pulsating sensation, moderate to severe pain intensity, and exacerbation headache with daily physical activity or avoidance of such activities due to headache. D. There should be at least 1 of the following 2 criteria present: nausea and/or vomiting, or photophobia and phonophobia. E. There was no alternative explanation that better accounts for the headaches in ICHD-3.

Inclusion criteria: (1) patients who were 14-65 years old; (2) patients who met the above diagnostic criteria for migraine without aura; (3) patients who were diagnosed as positive by TCM; (4) patients who were suffering from a

Table 1. Baseline characteristics of the subjects

Characteristics	Intervention group 1	Intervention group 2	Control group 3	F/X^2	P
N	60	60	60		
Age, years	38.55±12.24	40.45±12.95	38.27±13.54	0.506	0.604
Gender, M/F	19/41	21/39	20/40	0.150	0.928
Disease duration, years	13.57±8.08	15.68±8.42	14.45±8.66	0.962	0.384
Disease Location, N%				4.386	0.356
Left side	16 (26.6%)	13 (21.6%)	17 (28.3%)		
Right side	22 (36.7%)	28 (46.7%)	17 (28.3%)		
Bilateral	22 (36.7%)	19 (31.7%)	26 (43.4%)		
Body mass index, kg/m^2	22.49±4.04	23.00±4.90	22.59±4.12	0.223	0.800
Basic vitals					
SBP, mmHg	136.55±21.15	136.10±20.24	137.47±23.74	0.061	0.940
DBP, mmHg	73.95±9.78	72.83±10.54	73.98±10.10	0.250	0.779
HR, times/min	96.12±21.35	103.47±24.73	102.10±25.07	1.621	0.201
RR, times/min	20.87±4.70	21.10±4.64	21.68±5.01	0.463	0.630
Accompanying symptoms, N%					
Nausea or vomiting	49 (81.7%)	54 (90.0%)	49 (81.7%)	2.115	0.347
Photophobia or phonophobia	49 (81.7%)	54 (90.0%)	53 (88.3%)	2.019	0.364
Basic diseases, N%					
Cervical spondylosis	11 (18.3%)	11 (18.3%)	13 (21.7%)	0.284	0.868
Hypertension	14 (23.3%)	12 (20.0%)	20 (33.3%)	3.037	0.219
Diabetes	10 (16.7%)	11 (18.3%)	10 (16.7%)	0.078	0.962
Coronary heart disease	9 (15.0%)	9 (15.0%)	9 (15.0%)	0.000	1.000
Chronic bronchitis	9 (15.0%)	9 (15.0%)	8 (13.3%)	0.090	0.956
Asthma	9 (15.0%)	8 (13.3%)	11 (18.3%)	0.592	0.744
Chronic gastritis	14 (23.3%)	15 (25.0%)	14 (23.3%)	0.061	0.970
Chronic colorectitis	10 (16.7%)	9 (15.0%)	11 (18.3%)	0.240	0.887
Chronic cholecystitis	12 (20.0%)	9 (15.0%)	11 (18.3%)	0.532	0.766
Renal insufficiency	7 (11.7%)	10 (16.7%)	9 (15.0%)	0.629	0.730
Stable tumor	10 (16.7%)	9 (15.0%)	9 (15.0%)	0.085	0.959
Lifestyle habits, N%					
Staying up late (>23PM)	32 (53.3%)	38 (63.3%)	35 (58.3%)	1.234	0.539
Long working hours (>8 h/d)	46 (76.7%)	47 (78.3%)	43 (71.7%)	0.782	0.676
Children's educational issues	32 (53.3%)	30 (50.0%)	29 (48.3%)	0.311	0.856

Note: SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RR, respiratory rate.

headache attack at the time of treatment, and did not take painkillers for pain relief; (5) patients with complete clinical information.

Exclusion criteria: (1) patients with cardiovascular or cerebrovascular diseases, or severe primary diseases of key organs; (2) patients with history of nervous system organic diseases or psychosis; (3) patients with difficulty in understanding and describing headache conditions, or with poor compliance; (4) patients who were breastfeeding or pregnant; (5) patients with significant clinical data deficiencies.

Treatment methods

Study interventions

All medical personnel participating in this research program were from the front line of clinical practice, have received formal education in TCM schools, and have worked in emergency departments for over 5 years. They have all received training, including diagnostic criteria for migraine, migraine types, standard process of bloodletting, and auricular acupressure. To achieve the standardization and homo-

geneity of the TCM external treatment, all the external TCM treatment procedures were conducted by members of the TCM team.

The control group were administered Fenbid 0.3 g (Ibuprofen Sustained Release Capsules, Zhongmei Tianjin Smith Kline Pharmaceutical Co., Ltd.) orally. Patients with nausea symptoms received intramuscular injection of Metoclopramide Hydrochloride 10 mg/1 ml (Metoclopramide, Chengdu Better Pharmaceutical Co., Ltd.).

The intervention group 1 received auricular acupressure + Tongtian Oral Liquid. The auricular acupressure acupoints include: endocrine, both sides of Shenmen, subcortex, and sympathetic. Endocrine is the 18th area of the conchae, located in the notch between the screens, the front and lower end of the cavity of the conchae, 0.2 cm away from the edge of the notch between the screens. Shenmen is located in the posterior upper third of the triangular fossa. The subcortex is on the inner side of the tragus, at the midpoint of the inner surface of the outermost lower 1/3 of the antitragus, the 4th area of the antitragus. Sympathy is the front end of area 6 of the antihelix, in the area where the tail of the lower foot of the helix intersects the inner edge of the helix. For the operations, the patients were asked to take a seat. The operator used a probe to locate the acupoints. Reaction points could be seen in the relevant ear acupoints of the human body because of the condition of the illness. Optimal therapeutic effect can be obtained by directly stimulating such reaction points. The size and shape of each person's ears are different. The area where the auricular points are located is often larger than the reaction point. We used the probe to locate the reaction point before pressing the needle. The specific operations were as follows. The treatment personnel secured the upper back of the patient's auricle with both hands and held the probe stick. They applied uniform pressure from top to bottom to identify the reaction points. They confirmed the positive reaction points found by the naked eye. When locating the acupoints the patients were asked whether they felt soreness, swelling, or pain. A 75% ethanol swab was used to disinfect the entire auricle skin thoroughly, moving twice from top to bottom and from the inside to the outside. After the disinfection, the pressing needle was applied on the corresponding auricular points to provide appropriate massage. After the initial treatment, the patients were instructed to press the needle by themselves and retain the needle according to their own tolerance. The number of treatments was one time. Tongtian Oral Liquid produced by Taiji Group Chongqing Fuling Pharmaceutical Factory Co., Ltd. was administered 10 ml/time, 3 times/day for 1 month.

The intervention group 2 received Jing acupoint bloodletting + Tongtian Oral Liquid. Jing acupoint bloodletting selected Jing acupoints Guanchong (**Figure 1A**) and Zuqiaoyin (**Figure 1B**). Guanchong can be found when patients sit upright or lie on the back with palms down. It is on the ulnar side of the distal segment of the ring finger, 0.1 cun away from the corner of the nail root. Zuqiaoyin can be found when patients are lying on the back. It is on the outside of the fourth toe, 0.1 cun away from the corner of the nail. After locating the acupoints, the operator kneaded the first knuckle the ring finger on patient's ring finger of the diseased side to promote the blood circulation, and standardized disinfection was performed on the finger acupoints. A disposable peripheral blood collection device was used to prick the Guanchong point quickly and accurately for bloodletting, usually 10 to 30 drops. The volume of bloodletting was flexibly determined according to the patient's condition and changes of blood color. If bloodletting was blocked, the operator could rub the patient's fingers and administer local compression. After the operation, the acupoints were pressed shortly with a sterile cotton ball. The bloodletting operation was performed in the same way at Zuqiaoyin. The number of treatments is one time. The usage of Tongtian Oral Liquid was the same as that in the intervention group 1.

Outcome measures

Primary outcome measures: ① VAS (visual analog scale) score. VAS [10] was used to assess pain intensity after the intervention. The observation time points were 5 minutes before the intervention, and 0.5 h, 1 h, and 2 h after the intervention. VAS was scored on a scale of 0-10. Patients could move and locate on the scale according to their own actual feeling of pain. The nurse recorded the specific pain score according to the position on the scale. ② Immediate analgesic efficacy. The

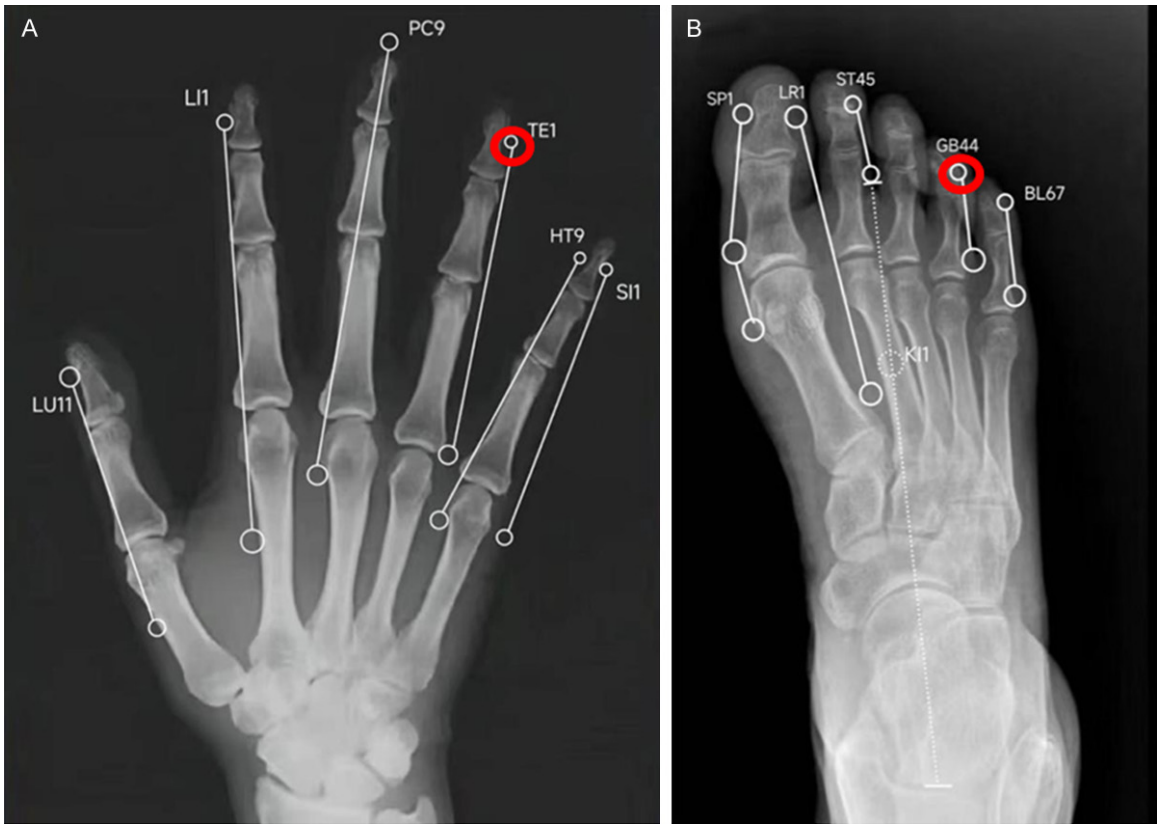

Figure 1. Acupoint. A: Guan Chong acupoint; B: Zu Qiao Yin acupoint.

pain relief within 60 minutes was evaluated with a total score of 0-10 points, with 0 point, 1-3 points, 4-6 points, and 7-10 points for no pain, mild pain, moderate pain, and severe pain, respectively. No pain or mild pain within 60 minutes was considered effective immediate pain relief. ③ Dynamic analgesic time curve analysis. Taking immediate analgesic efficacy as the endpoint event, the time required for the VAS score to return to mild pain was recorded, and the dynamic changes of analgesic time were compared. ④ Scores of pain questionnaire. The short-form McGill pain questionnaire (SF-MPQ) [11] was used to evaluate the pain in patients 5 minutes before treatment and 120 minutes after treatment. The main components of MPQ are pain rating index (PRI), VAS and present pain intensity (PPI). The PRI consists of 2 parts, sensory (11 items) and affective (4 items). Based on the severity, the scores range from 0-3 points, indicating none (0 point), mild (1 point), moderate (2 points), heavy (3 points) pain, respectively. VAS was the self-assessment of headache intensity. PPI consists of 6 levels, no pain (0 point), mild (1 point), discomforting (2 points), distressing (3 points), horrible (4 points), and excruciating (5 points). The three scores were added up to calculate the total score (T), with higher scores indicating more severe pain.

Secondary outcome measures: ① Remaining symptoms after 2 hours of treatment: included fatigue, lethargy, nausea, and vomiting. ② Oral ibuprofen usage within 24 hours of treatment. Ibuprofen was taken 200 mg orally once, with a maximum dose within 24 hours not exceed 800 mg. ③ The number of cases with pain recurrence at least 1 time within 24 hours of treatment. ④ The number of pain episodes within one month: the average number of pain episodes of patients in each group within one month. ⑤ Risk factors affecting the number of pain attacks. Based on the average number of pain attacks in each group within one month, the patients were redivided into a good prognosis group (≤2 times) and a poor prognosis group (>2 times). Factors including patient age, grouping, disease duration, body mass index (BMI), underlying disease, and residual symp-

toms after treatment were included in the univariate analysis. The factors with P<0.1 were subjected to further stepwise regression analysis to identify the independent prognostic factors.

Safety observation

Adverse reactions related to the intervention were recorded, including allergy, syncope, and skin infection.

Statistical analysis

We performed efficacy analyses in the full analysis set. This included all the patients who received at least one treatment and had at least one efficacy measure. The last observation carried forward approach was utilized to impute missing data. We performed sensitivity analyses for each protocol set. This included all the patients without major protocol deviations. Safety analyses were performed in all the patients who had received at least one treatment.

The statistical tool used was SPSS26.0. Conventional numerical values were presented in the form of frequency and percentage. For measurement values, if the distribution was normal, the description form was mean ± standard deviation; if the distribution was skewed, the description form was median (interquartile range) [(M (IOR))]. Descriptive statistics were processed using the χ^2 test between the groups, and the pairwise test of the two groups was performed. For comparison of the means among multiple groups of measured data, multi-factor analysis of variance was used when the distribution was normal and the variance was homogeneous, and LSD test was used for pairwise comparison. Paired sample t-test was used for comparison before and after treatment within the group. If the distribution was skewed and the variance was uneven, multi-group independent sample rank sum (Kruskal-Wallis) test was used, and Mann-Whitney U test was used for comparison between two groups. The Kaplan-Meier survival curve analysis was used to analyze the immediate analgesic efficacy in different intervention groups. Log-Rank method was employed to compare the differences between the groups. The influencing factors were analyzed using the binary logistic regression analysis, using the factors with P<0.1 in the univariate regression analysis. All statistical tests were two-sided. The significant level of difference was set at P<0.05. The figures were plotted by GraphPadprism8.0.2 software.

Results

Participant characteristics

The study subjects were divided into three groups, with 60 cases in each group. The three groups were compared in terms of gender, age, disease location, duration of disease, basic vital signs, accompanying symptoms, underlying disease, and general information. The differences were not significant (P>0.05). See **Table 1**.

Pre- and post-treatment VAS/SF-MPQ scores in the three groups

There were no significant differences in the VAS and SF-MPQ scores between the two groups 5 minutes before the intervention (P>0.05). Compared with before the intervention, the VAS and SF-MPQ scores significantly decreased in all groups 2 hours after the intervention (P<0.01). Inter-group comparison found that the score decline rate in the intervention group 1 > that in the intervention group 2 > that in the control group, and the differences were significant (P<0.01). In terms of immediate analgesic efficiency within 60 minutes, intervention group 1 > intervention group 2 > control group (100% vs. 76.67% vs. 56.67%, P<0.001). See **Tables 2**, **3** and **Figure 2** for details.

Prognosis-related indicators

Comparing the residual symptoms after 2 hours of treatment, there were more cases of fatigue (P<0.001) and lethargy (P=0.031) occurred in the control group than in the intervention groups, but there was no significant difference in cases of lethargy between the two intervention groups. There was no significant difference in nausea and vomiting among the three groups (P=0.152). In terms of 24-hour ibuprofen usage, control group > intervention group 2 > intervention group 1 (P<0.001), and the differences between the groups were significant (P<0.01). In terms of the 24 h pain recurrence rate, the rate in the intervention group 1 was

Table 2. Pre- and post-treatment VAS/SF-MPQ scores in three groups (x±s)

Time point/Group	Intervention group 1	Intervention group 2	Control group 3	F/X^2	*P*
N	60	60	60		
VAS					
Before treatment	5.60±0.91	5.62±0.92	5.45±0.91	0.607	0.546
Difference after 120 minutes	-5.02±1.05	-4.40±1.26	-3.52±0.85	29.830	<0.001
Pairwise comparisons-mean (95% CI)	1 vs. 2 0.617 (0.23-1.00)	2 vs. 3 0.883 (0.50-1.27)	1 vs. 3 1.500 (1.11-1.89)		
P	0.002	<0.001	<0.001		
SF-MPQ					
Before treatment	14.87±1.01	15.15±1.27	15.17±1.49	1.045	0.354
Difference after 120 minutes	-10.77±2.74	-8.47±4.12	-5.52±3.56	33.484	<0.001
Pairwise comparisons-mean (95% CI)	1 vs. 2 2.3000 (1.03-3.57)	2 vs. 3 2.950 (1.68-4.22)	1 vs. 3 5.250 (3.98-6.52)		
P	<0.001	<0.001	<0.001		

Note: VAS, visual analogue scale; SF-MPQ, short-form McGill pain questionnaire.

Table 3. Dynamic analysis of 60-minute pain relief rates in the three groups

Group	N	Mean time to pain relief (95% CI) min	Median time to pain relief (95% CI) min	30-minute pain relief rate (%)	60-minute pain relief rate (%)
Intervention group 1	60	36.16 (34.46-38.86)	36.00 (33.47-38.52)	17 (28.33%)	60 (100.00%)
Intervention group 2	60	54.48 (47.43-61.52)	46.00 (35.88-56.11)	8 (13.33%)	46 (76.67%)
Control group 3	60	74.78 (65.69-83.87)	55.00 (50.25-59.74)	4 (6.67%)	34 (56.67%)

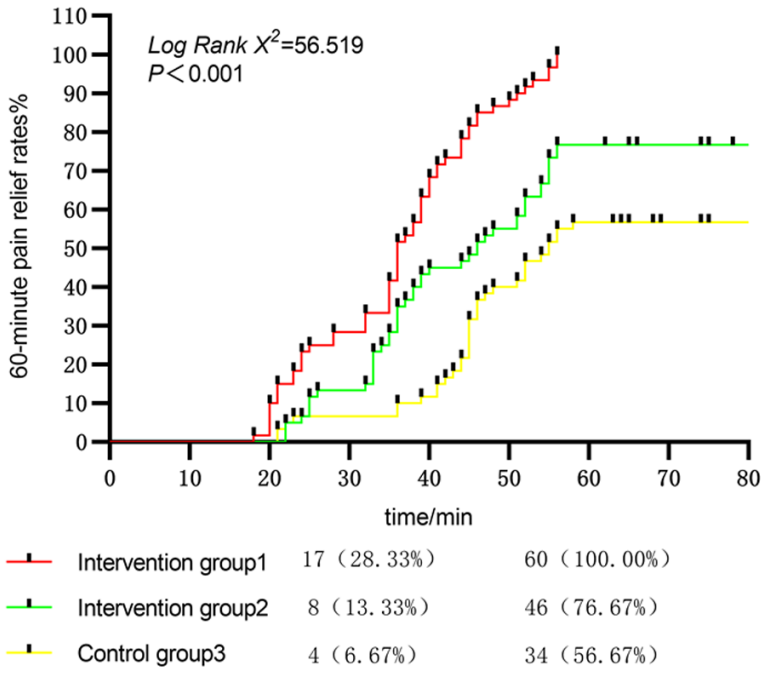

Figure 2. Comparison of dynamic 60-minute analgesic rates among the three groups.

significantly lower than that in the intervention group 2 and the control group (P<0.05). There was no significant difference between the intervention group 2 and the control group (P>0.05). The average number of headache attacks within 30 days was significantly higher in the control group than that in the intervention groups (P=0.012), but there was no significant difference between the two intervention groups (P=0.568). See **Table 4** for details.

Regression analysis of factors affecting the number of headache attacks within a month

According to the average number of headache attacks, the patients were redivided into a good prognosis group (≤2 times) and a poor prognosis group (>2 times). The course of disease, BMI, underlying diseases, lifestyle habits, and residual symptoms after treatment were included in the univariate regression analysis, and the factors

Table 4. Prognosis-related indicators

Group	Intervention group 1	Intervention group 2	Control group 3	F/X^2	*P*
N	60	60	60		
Fatigue after 2 h, N%	8 (13.3%)	13 (21.7%)	27 (45.0%)	16.534	<0.001
Pairwise comparisons *P*	1 vs. 2 0.230	2 vs. 3 0.007	1 vs. 3 <0.001		
Drowsiness after 2 h, N%	8 (13.3%)	7 (11.7%)	17 (28.3%)	6.917	0.031
Pairwise comparisons *P*	1 vs. 2 0.783	2 vs. 3 0.022	1 vs. 3 0.043		
Nausea or vomiting after 2 h, N%	10 (16.67%)	8 (13.33%)	16 (26.67%)	3.771	0.152
Pairwise comparisons *P*	1 vs. 2 0.609	2 vs. 3 0.068	1 vs. 3 0.184		
24 h Proportion of pain recurrence, N%	2 (3.30%)	7 (11.67%)	10 (16.67%)	5.767	0.056
Pairwise comparisons *P*	1 vs. 2 0.083	2 vs. 3 0.432	1 vs. 3 0.015		
24 h Ibuprofen dosage, mg	316.67±28.93	396.67±27.30	505.00±20.36	13.418	<0.001
Pairwise comparisons-mean (95% CI)	1 vs. 2 -80.000 (-152.02 to -7.98)	2 vs. 3 -108.333 (-180.35 to -36.32)	1 vs. 3 -188.333 (-260.35 to -116.32)		
P	0.030	0.003	<0.001		
30 d Number of episodes of headache	2.30±0.94	2.40±1.04	2.80±0.88	4.572	0.012
Pairwise comparisons-mean (95% CI)	1 vs. 2 -0.100 (-0.45 to 0.25)	2 vs. 3 -0.400 (-0.75 to -0.05)	1 vs. 3 -0.500 (-0.85 to -0.15)		
P	0.568	0.023	0.005		

with P<0.1 were subjected to further stepwise logistic regression analysis. It was found that age (OR=1.036, 1.006-1.068), BMI (OR=1.101, 1.008-1.201), hypertension (OR=2.879, 1.187-6.986), chronic gastritis (OR=2.839, 1.213-6.647), children with educational problems (OR=0.333, 0.164-0.676), and residual fatigue symptoms (OR=4.539, 1.828-11.271) were factors affecting the number of headache attacks within one month. It can be preliminarily concluded that older age, higher BMI, residual fatigue symptoms after the pain attacks, and basic diseases including hypertension and chronic gastritis were risk factors associated with worsened prognoses and more frequent attacks. Some patients with family educational problems have a risk of poor prognosis due to high mental stress. This requires more research and attention. See **Table 5** for details.

Discussion

This study included patients with migraine in the acute stage treated with conventional anti-inflammatory medicine, bloodletting at Jing acupoint + Tongtian Oral Liquid, and auricular acupressure + Tongtian Oral Liquid, respectively. The immediate analgesic efficiency and the recurrence of pain were compared among the groups. The auricular acupressure + Tongtian Oral Liquid group demonstrated significant advantages in the immediate analgesic efficiency than the other two groups. This included a faster average and median time for pain relief within 60 minutes. After 2 hours of treatment, the auricular acupressure + Tongtian oral liquid group and the Jing point bloodletting + Tongtian oral liquid group exhibited fewer side effects of fatigue and drowsiness than the conventional western medicine group. These results suggest that TCM external therapy combined with internal therapy has considerable therapeutic effect on migraine. Auricular acupressure + Tongtian Oral Liquid are favorable for treating migraine in the acute stage because of its immediate efficiency in pain relief.

In "Auricular Point Diagnosis and Therapeutics" [12], "pain relief" is the first among the "ten stops" of auricular point functions. Based on the anatomical location, it can be deduced that there are corresponding nerves at the auricular points, including the greater auricular nerve and auricular temporal nerve at Shenmen point, trigeminal nerve and lesser occipital nerve at sympathetic points, lingual nerve and vagus nerve distributed at subcortical points, and mixed branches of vagus nerve and facial nerve distributed at endocrine points. Stimulation of auricular points can indirectly regulate the function of the central nervous system and cerebral cortex, relieving headaches. From the analysis of the efficacy of auricular points, Shenmen point, subcortical

Table 5. Results of univariate and multivariate logistic regression analyses of factors influencing the number of headache attacks within one month

Factors	Univariate analysis					Multivariate analysis				
	β	*P*	Exp (β)	95% CI		β	*P*	EXP (β)	95% CI	
Group		0.026								
Group 1 vs. 3	-1.012	0.009	0.364	0.169	0.781					
Group 2 vs. 3	-0.811	0.038	0.444	0.207	0.956					
Age	0.021	0.088	1.021	0.997	1.045	0.035	0.020	1.036	1.006	1.068
Disease duration	0.018	0.334	1.018	0.982	1.055					
BMI	0.093	0.013	1.097	1.020	1.180	0.096	0.032	1.101	1.008	1.201
Cervical spondylosis	0.331	0.401	1.392	0.643	3.012					
Hypertension	1.324	0.001	3.759	1.683	8.394	1.057	0.019	2.879	1.187	6.986
Diabetes	0.259	0.528	1.296	0.580	2.897					
Chronic gastritis	0.729	0.056	2.073	0.983	4.375	1.043	0.016	2.839	1.213	6.647
Chronic cholecystitis	0.319	0.433	1.376	0.619	3.061					
Renal insufficiency	-0.268	0.530	0.765	0.332	1.765					
Stable tumor	0.063	0.882	1.065	0.467	2.428					
Staying up late (>23PM)	0.339	0.271	1.403	0.768	2.564					
Long working hours (>8 h/d)	-0.633	0.090	0.531	0.256	1.103					
Children's educational issues	-0.951	0.002	0.386	0.209	0.714	-1.098	0.002	0.333	0.164	0.676
Fatigue after 2 h	1.579	0.000	4.851	2.110	11.149	1.513	0.001	4.539	1.828	11.271
Drowsiness after 2 h	0.489	0.240	1.631	0.721	3.685					
Nausea or vomiting after 2 h	0.274	0.489	1.316	0.605	2.860					

point, and sympathetic point can all regulate the autonomic function of nerves [13]. Stimulating Shenmen point can effectively regulate the central nervous system, and induce anti-inflammatory, analgesic and sedative effects. The subcortical point is a high-level nerve activity center. This has an anti-inflammatory and analgesic effect. The sympathetic point has the function of regulating autonomic nerve function, and its effects include promoting blood circulation and relieving spasm. Endocrine has the functions of soothing the liver and regulating qi, promoting blood circulation, dredging collaterals, and relieving pain. Auricular acupressure is to stimulate ear acupoints, and is a major part of acupuncture and moxibustion. With the development of society, the tools used for acupoint stimulation have evolved from simple "Wangbuliuxing seeds" to press needles (a kind of intradermal microneedle tool). As a TCM external treatment for migraine, auricular acupressure has been confirmed by clinical studies to be effective [14-16]. Compared with the previous seed stimulation and auricular acupressure, the auricular acupressure using needles has greater advantages. The pressing needles are small and can directly penetrate the subcutaneous tissues at the relevant auricular point to precisely stimulate the point. It is not easy to fall off, with good practicality. Bloodletting therapy was first seen in the "Huangdi Neijing" as "when the asteroid is old, get rid of it, bad blood will come out", "whenever a disease is cured, the blood must be removed first". The application of this therapy can alleviate blood congestion in the body, relieve pain, and promote new blood production, improving symptoms and addressing underlying health conditions. It has been proven effective by modern clinical research [17]. By regulating the local microcirculation, the blood flow velocity is improved. This addresses the insufficient blood supply to the brain and vasospasm, and alleviate the cerebral ischemia and hypoxia, alleviating or curing the disease. Jing acupoints are located on the extremities, with rich surrounding microvessels and peripheral nerves. It is a commonly used treatment site for bloodletting therapy. Jing acupoint bloodletting therapy is a routine treatment for various pain diseases in the external treatment of TCM [18-20]. Tongtian oral liquid is derived from the addition and subtraction of "Chuanxiong Tea Tiaosan" in the Ming Dynasty,

with Chuanxiong, Chishao, Gastrodia elata, Qianghuo, Angelica, Fangfeng, chrysanthemum, Asarum, mint, tea, and licorice as the main ingredients. In TCM, it is believed that Fengxie is the main exogenous evil that causes migraine. Tongtian Oral Liquid can relieve pain by dispelling Fengxie. Modern pharmacological research found that [21, 22] gastrodin, myrcene and succinic acid in Tongtian Oral Liquid could play an anti-oxidation role, reducing vascular resistance, and increasing cerebral blood flow. Xue's research found that [23] Tongtian Oral Liquid may regulate pain by affecting plasma β-endorphin.

A meta-analysis showed that [24] the total response rate and cure rate of auricular point sticking and pressing in the treatment of migraine were higher than those of other treatments (western medicine treatment and TCM internal treatment). Auricular acupressure has a stronger pain relief effect. A previous study recruited 45 subjects [25] for a study of shoulder pain, with 30 subjects in the treatment group received acupressure on auricle points representing the shoulder region (the scapular fossa), and 15 subjects in the control group received acupressure on auricular areas unrelated to the shoulder. In another study on migraine [26], 80 migraineurs were divided into two groups, with the intervention group receiving auricular acupuncture and the control group received only conventional treatment, and auricular acupuncture was found to be effective in pain relief.

Our study compared the TCM treatments with western medicine. It also compared the two TCM treatments (auricular acupressure + Tongtian Oral Liquid and Jing point bloodletting + Tongtian Oral Liquid). Our results confirmed the effectiveness of TCM treatments, and highlighted the advantages of auricular acupressure.

Common risk factors for migraine include unmodifiable genetics, gender, age, modifiable drug overuse, obesity, and stressful life events [27]. In our study, we found that high blood pressure, chronic gastritis, children's educational problems, and residual fatigue symptoms were related to the onset of migraine. These results serve as a warning and sign of early clinical intervention.

One of the strengths of this study is the design of a control group and two experimental groups with different interventions. We compared the auricular acupressure + Tongtian Oral Liquid and Jing acupoint bloodletting + Tongtian Oral Liquid with traditional ibuprofen treatment to identify their different performance in immediate analgesic efficacy of migraine, and the frequency and severity of migraine attacks within one month. This design can observe the effects of different measures, and facilitate the clinical acceptance of auricular acupressure and bloodletting therapy in emergency patients. Compared with painful treatment methods including acupuncture and bloodletting, patients are more likely to accept the painless operation, auricular acupressure. This increases the patient compliance. This study had certain limitations. This was not a clinical trial. A randomized controlled design was not achieved. The study failed to have a placebo group. All the cases enrolled were from the same healthcare facility. In future studies, the study samples and regions should be expanded to conduct a multicenter randomized controlled study. Study factors of blinding and placebo should be included to increase the credibility of the results.

Conclusion

In conclusion, for the treatment of migraine without aura in the acute stage, auricular acupressure + Tongtian Oral Liquid can achieve better immediate analgesic effect and longer-lasting pain relief as compared with conventional treatment and bloodletting at Jing acupoints + Tongtian Oral Liquid. Bloodletting at Jing acupoints and auricular acupressure plus Tongtian Oral Liquid can reduce the number of pain attacks. We found that auricular acupressure combined with Tongtian oral liquid is promising for the immediate treatment and prognosis of acute migraine without aura. This combination was associated with advantages of effectiveness, quick onset, and convenience. It should be promoted in clinical practice.

Acknowledgements

This study was supported by Jiangsu Provincial Hospital of Traditional Chinese Medicine Department Director Special Fund (Y2021ZR-10) and Jiangsu Province Traditional Chinese

Medicine Science and Technology Development General Project (MS2022018) and National Clinical Research Base of Traditional Chinese Medicine (Jiangsu Hospital of Traditional Chinese Medicine) open fund (JD2022-SZ03).

Disclosure of conflict of interest

None.

Address correspondence to: Tao Guo and Sicheng Yuan, Department of Emergency, Affiliated Hospital of Nanjing University of Chinese Medicine (Jiangsu Province Hospital of Chinese Medicine), No. 155, Hanzhong Road, Nanjing 210000, Jiangsu, China. Tel: +86-025-86610842; E-mail: guotaojsszyy@163.com (TG); 1491103741@qq.com (SCY)

References

[1] GBD 2021 Anaemia Collaborators. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990-2021: findings from the Global Burden of Disease Study 2021. Lancet Haematol 2023; 10: e713-e734.

[2] GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol 2021; 20: 795-820.

[3] Sudershan A, Mahajan K, Singh K, Dhar MK and Kumar P. The complexities of migraine: a debate among migraine researchers: a review. Clin Neurol Neurosurg 2022; 214: 107136.

[4] Wang X, Na W, Yang Y, Zhang W, Zhao J, Zhang T, Zhou Y, Liu H, Zhao D and Yu S. Should migrate without aura be further divided? A study of 1444 female patients with migrate without aura. J Headache Pain 2023; 24: 20.

[5] GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry 2022; 9: 137-150.

[6] Natbony LR and Zhang N. Acupuncture for migraine: a review of the data and clinical insights. Curr Pain Headache Rep 2020; 24: 32.

[7] Zhang F, Shen Y, Fu H, Zhou H and Wang C. Auricular acupuncture for migraine: a systematic review protocol. Medicine (Baltimore) 2020; 99: e18900.

[8] Tang Q. Clinical efficacy analysis of auricular point pressing acupuncture for migraine. Health Care Literature 2021; 22: 187-188.

[9] Headache and Sensory Disorders Committee of the Chinese Society of Research Hospitals, Neurologists Branch of the Chinese Physicians Association. Guidelines for the diagnosis and treatment of migraine in China (2022 edition). Chinese Journal of Pain Medicine 2022; 28: 881-898.

[10] Lucas C, Romatet S, Mekiès C, Allaf B and Lantéri-Minet M. Stability, responsiveness, and reproducibility of a visual analog scale for treatment satisfaction in migraine. Headache 2012; 52: 1005-1018.

[11] Bakhtadze MA, Lusnikova IV, Kuzminov KO and Bolotov DA. The Second Short Form of the McGill Pain Questionnaire as the useful additional tool for differential diagnostics of migraine and cervicogenic headache. Zh Nevrol Psikhiatr Im S S Korsakova 2021; 121: 70-76.

[12] Huang CL. Therapeutics of Auricular Acupuncture and Moxibustion. Beijing: Science and Technology Literature Publishing House; 1991. pp. 37.

[13] Mao JJ, Liou KT, Baser RE, Bao T, Panageas KS, Romero SAD, Li QS, Gallagher RM and Kantoff PW. Effectiveness of electroacupuncture or auricular acupuncture vs usual care for chronic musculoskeletal pain among cancer survivors: the PEACE randomized clinical trial. JAMA Oncol 2021; 7: 720-727.

[14] Sun S, Liu L, Zhou M, Liu Y, Sun M and Zhao L. The analgesic effect and potential mechanisms of acupuncture for migraine rats: a systematic review and meta-analysis. J Pain Res 2023; 16: 2525-2542.

[15] Wang Y, Du R, Cui H, Zhang L, Yuan H and Zheng S. Acupuncture for acute migraine attacks in adults: a systematic review and meta-analysis. BMJ Evid Based Med 2023; 28: 228-240.

[16] Guo W, Cui H, Zhang L, Du R, Yuan H and Zheng S. Acupuncture for the treatment of migraine: an overview of systematic reviews. Curr Pain Headache Rep 2023; 27: 239-257.

[17] Li R, Lu Y, Wang MM and Yang DH. Bloodletting at auricular dorsal vein combined with auricular point sticking for menstrual migraine of qi stagnation and blood stasis and its effect on serum levels of E2 and 5-HT. Zhongguo Zhen Jiu 2023; 43: 427-431.

[18] Wang H, Wan R, Chen S, Qin H, Cao W, Sun L, Shi Y, Zheng Q and Li Y. Comparison of efficacy of acupuncture-related therapy in the treatment of postherpetic neuralgia: a network meta-analysis of randomized controlled trials. Evid Based Complement Alternat Med 2022; 2022: 3975389.

[19] Lu H, Liu W, Fan Y, Lv W, Yang D, Liu C and Lin F. Efficacy and safety of Qinpi Tongfeng formula

combined with bloodletting therapy in the treatment of acute gouty arthritis: a study protocol for a randomized controlled trial. Evid Based Complement Alternat Med 2022; 2022: 3147319.
[20] Li SH, Hu WS, Wu QF and Sun JG. The efficacy of bloodletting therapy in patients with acute gouty arthritis: a systematic review and meta-analysis. Complement Ther Clin Pract 2022; 46: 101503.
[21] Zhen-Min XU, Min J, Xiao L, Jing-Jing W, Guo-Jing FU, Lin L, Qian C, Yan LU, Yun-Ling Z and Xing L. Clinical practice guideline for migraine with traditional Chinese medicine (draft version for comments). Zhongguo Zhong Yao Za Zhi 2020; 45: 5057-5067.
[22] Min J, Yan LU, Yun-Ling Z, Xing L, Xiao L, Wei S, Jing-Jing W, Lin L, Qian C and Guo-Jing FU. Network meta-analysis of oral Chinese patent medicine in treatment of migraine. Zhongguo Zhong Yao Za Zhi 2020; 45: 5068-5082.
[23] Dongjie S, Rajendran RS, Xia Q, She G, Tu P, Zhang Y and Liu K. Neuroprotective effects of Tongtian oral liquid, a traditional Chinese medicine in the Parkinson's disease-induced zebrafish model. Biomed Pharmacother 2022; 148: 112706.
[24] Xu J, Zhang FQ, Pei J and Ji J. Acupuncture for migraine without aura: a systematic review and meta-analysis. J Integr Med 2018; 16: 312-321.
[25] Lovato A, Postiglione M, Gagliardi G, Parmagnani M, Biral M and Ceccherelli F. Needle contact test in auricular acupuncture for shoulder pain and where effective auricular acupoints identified are positioned on the map: a controlled study. Eur J Transl Myol 2023; 33: 11113.
[26] Habibabadi MR, Ashtari F and Raeisi I. Effect of auricular acupuncture with semi-permanent ear needles on controlling migraine symptoms: a single-blind randomized clinical trial. J Acupunct Meridian Stud 2021; 14: 58-66.
[27] Yang Y and Cao Y. Rising trends in the burden of migraine and tension-type headache among adolescents and young adults globally, 1990 to 2019. J Headache Pain 2023; 24: 94.