

Immediate analgesic effect of cheek acupuncture vs etoricoxib for patients with acute gouty flare: a randomized controlled trial

Yuping Lin

Guangdong Provincial Hospital of Chinese Medicine

zhaojun Yang

ShenZhen People's Hospital

Yehao Luo

Guangdong Provincial Hospital of Chinese Medicine

Qiaoyun Liu

University of Chinese Medicine

Lu Sun

Guangdong Provincial Hospital of Chinese Medicine

Guanjie Fan

fanguan.jie@gzucm.edu.cn

Guangdong Provincial Hospital of Chinese Medicine

Research Article

Keywords: Cheek acupuncture, acute gouty flare, Immediate analgesic effect, etoricoxib

Posted Date: September 23rd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10992806/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Objective

Given the paucity of effective therapies for pain relief of acute gouty flare (AGF), the immediate analgesic effect of cheek acupuncture was evaluated in patients with AGF.

Methods

This randomized controlled trial evaluated the immediate analgesic effect of cheek acupuncture (CA, intervention, $n = 38$) compared with etoricoxib (EC, control, $n = 38$). Visual Analogue Scoring (VAS) and the degree of pain relief were assessed before treatment, 0 min, 30 min, 1 h and 2 h after the start of treatment. Joint tenderness was assessed before and 2h after treatment. Patient's feedback was collected 2h after treatment.

Results

Altogether, 76 persons received once treatment and completed the study. At 2 h after treatment, group CA exhibited significant decrease in VAS, the degree of pain relief, joint tenderness and better patient's feedback when compared to group EC ($P < 0.001$). Following intervention, the VAS scores in the CA group decreased rapidly, dropping to 4 (4, 5) at 0 minutes post-treatment and reaching a minimum of 2 (2.5, 3) at 1 hour, however, there was a mild increase in the VAS score to 2 (3, 4) at the 2-hour time point. In the EC group, the VAS score began to decrease at 1 hour post-treatment, dropping to 6 (6, 8), and was followed by a further decrease to 6 (5, 7) at the 2-hour mark. There were 2 adverse events occurred in group EC, while no adverse events were observed during the trial in group CA.

Conclusions

CA provides quick pain relief for gout sufferers. Compared to oral pain medication, it effectively eliminates the time lag between consultation and the medication's onset of action, thus exhibiting a more significant advantage in improving the satisfaction of the consultation.

Trial registration:

Preregistered at Clinicaltrials.gov (<https://register.clinicaltrials.gov>) on 21 August 2023. Clinical trial number: NCT06001112.

Introduction

As one of the oldest diseases in the world, gout is the most prevalent form of inflammatory arthritis ^[1, 2]. Published data indicate that gout prevalence has increased markedly in the last three decades, with the most significant rise occurring in high-income regions ^[3]. It is estimated that the global prevalence of gout will reach 96 million by 2050, making gout the second most common metabolic disease after diabetes in the 21st century ^[4]. The clinical manifestations of acute gouty flare (AGF) mainly include pain, swelling, fever, redness, and joint hypermobility ^[5]. Once gout occurs, pain peaks within 24 hours and reaches 7 points or more on a 0–10 scale ^[6, 7]. In the 1990s, the American Pain Society aggressively promoted the concept of pain as the fifth vital sign ^[8]. Severe pain dramatically affects patients' daily activities and quality of life ^[9].

Outpatients with AGF often suffer from pain. Colchicine, nonsteroidal anti-inflammatory drugs (NSAID), and corticosteroids are routinely used to relieve pain in adults with acute gout episodes ^[10]. The patient visits the doctor, obtains a prescription, and pays for the medication. After taking it, they still must wait at least 2 hours before experiencing pain relief ^[11]. There is a time gap between the consultation and the initial of pain relief, and the speed of pain relief is an important factor for clinicians to consider.

Treatments that provide immediate pain relief may help patients with gout. Studies reported that some external Chinese medical treatments, such as bloodletting and fire needling, quickly reduce pain in the acute phase of gout ^[12, 13]. Acupuncture has been employed for millennia in China and other countries for the treatment of a plethora of medical conditions. Its efficacy in the management of gouty arthritis has been demonstrated in clinical trials ^[14]. Cheek acupuncture (CA) is a therapy that involves needling in the cheeks and was invented by Prof. Yongzhou Wang ^[15]. It involves inserting needles into specific points on the cheek and requires only a seated position in the office, without the need for a specialized consultation bed. Moreover, the needles are very thin, and the cannula method of needle insertion is less painful than the traditional acupuncture method, making it easier for patients to accept. Numerous clinical studies have shown that CA is effective in pain disorders, achieving an immediate pain relief rate of up to 72.5%, and is effective across different ethnic groups ^[16].

Our initial clinical observations indicated that AGF patients undergoing CA during their first consultation experienced varying degrees of analgesic benefit, which significantly improved their overall satisfaction. To further evaluate the immediate efficacy and analgesic effect of CA in managing AGF, we designed a prospective, randomized, controlled clinical trial. In this study, etoricoxib, a rapidly acting and highly gastrointestinal-safe NSAID with high selectivity for COX-2 inhibition, was employed as the comparative agent. This article examines whether CA provides superior immediate pain relief compared to EC.

Methods

Study design

This was a single-center randomized, controlled, prospective clinical trial in which 76 AGF patients were randomized (in a 1:1 ratio) to either the CA group (intervention, n = 38) or the EC group (control, n = 38). The

study was conducted between September 2023 and December 2024 at a single site in China (Guangdong Provincial Hospital of Chinese Medicine). It was approved by the Ethics Committee and preregistered at ClinicalTrials.gov (NCT06001112). Every participant received information about the study objectives and experimental procedures and signed an informed consent form.

Recruitment and Participants

Patients with AGF aged 18 to 75 years were recruited from the Gout Chronic Disease Management Clinic based on inclusion and exclusion criteria. The diagnosis of gout was confirmed by an endocrinologist, an orthopedic surgeon, or a rheumatologist. Clinicians explained the study orally to the participants and then obtained their written informed consent. Participants' privacy was strictly maintained.

The inclusion criteria were as follows:

1. Meet the diagnostic criteria for acute gouty arthritis, with attacks occurring in either the unilateral ankle or the first metatarsophalangeal joint;
2. Age between 18 and 75 years, regardless of gender;
3. The gouty arthritis attack occurred within the past 48 hours;
4. No prior treatment with targeted topical therapies or self-administered medications, including colchicine, anti-inflammatory drugs, hormones, or herbal remedies;
5. Patients agree to comply with the clinician's treatment plan.

The exclusion criteria were as follows:

1. Pregnant or breast-feeding;
2. Patients with malignant tumors; severe dysfunction of the heart, liver, or kidneys; diabetes mellitus; or hypertension;
3. Mental disorders that prevent the patient from understanding the nature, scope, and possible outcomes of the study, or from following the doctor's advice;
4. Allergy to any components of the drug used in this study;
5. Patients with active peptic ulcers/bleeding, or previous recurrent ulcers/bleeding;
6. History of asthma, urticaria, or allergic reactions induced by aspirin or other nonsteroidal anti-inflammatory drugs;
7. Congestive heart failure (New York Heart Association cardiac function class II-IV).

Randomization and masking

The block randomization sequence was generated by SAS 9.2 software (SAS Institute Inc., Cary, NC, USA) with a block size set at four. Eligible participants were randomly allocated to either the CA group or the EC group at a ratio of 1:1. This was done through the Central Randomization Management System, developed by the Key Unit of Methodology in Clinical Research (KUMCR). The procedure was conducted by an independent staff member of the KUMCR of Guangdong Provincial Hospital of Chinese Medicine, and

allocation concealment was maintained prior to assignment. The randomization allocation results were released through the Central Randomization Management System. The researchers conducted clinical treatment observations according to the intervention plan corresponding to the randomization number. This study was not blinded because physicians needed to administer oral medications or acupuncture treatments to subjects according to the predetermined grouping results.

Sample size

Based on the preliminary experiment, the visual analogue scale (VAS) score at 2 hours post-treatment was designated as the primary outcome. The estimated mean VAS score in the control group was 4.2, with an expected reduction of 1.5 in the treatment group. The standard deviation for both groups was 1.8. Using PASS 8.0 software for sample size calculation, with a two-sided α of 0.05, power (1- β) of 0.8, a δ of 0.4, and 1:1 allocation ratio, a minimum of 34 participants per group was required. Accounting for a 10% anticipated dropout rate, the final sample size was adjusted to 38 participants per group, yielding a total sample size of 76 participants for the study.

Outcomes

The VAS score 2 hours after treatment was the primary outcome measure in this study. VAS is a 10-cm horizontal or vertical line divided into 10 equal segments, where the left (or top) end indicates “no pain” and the right (or bottom) end indicates “severe pain”. The VAS pain scale ranges from 0 to 3 for no or mild pain, from 4 to 6 for moderate pain, and from 7 to 10 for severe pain^[17]. Participants were asked to mark the pain level he/she felt with an “I” on this line. To reduce subjective errors when comparing before and after measurements, patients were instructed to mark only on unmarked sections of the line during each assessment. Dynamic VAS change curves were recorded at baseline (before treatment), and at 0, 30, 60, and 120 minutes after treatment initiation.

Secondary outcome measures include joint tenderness and patient feedback. The degree of joint tenderness was recorded using a 5-point Likert scale before treatment and again 2 hours after the start of treatment. An 8-point patient global assessment of treatment response score was used to record patient feedback 2h after the start of treatment.

Interventions

Cheek Acupuncture group

Patients received CA treatment from the same professionally trained acupuncturist. This approach ensured consistent selection of acupuncture points and uniform treatment procedures. The acupuncture points and procedures adhered strictly to the guidelines outlined in “CA Therapy”^[15]. Sterile and disposable acupuncture needles were used in this trial (Bond Medical Instrument Co., Ma’anshan, China). During the treatment, the patient assumed a supine position. After routine local skin disinfection, the needle was

promptly inserted through the skin into the acupuncture point. In this study, selected acupuncture points include bilateral head points, bilateral upper energizer points, bilateral middle energizer points, bilateral lower energizer points, affected unilateral ankle point, and affected unilateral foot point. Table 1 displays the acupoint locations utilized in this study. In order to strengthen the local analgesic effect, additional needles closer to the acupoint were required, using the triangular needle strengthening method (Fig. 1).

Table 1
Locations of acupuncture points in this study.

Name	Orientation
Head point CA-1	1 inch above the upper edge of the middle point of the zygomatic arch
Upper energizer point CA-2	The cross of the posterior coronoid of the mandible and the lower edge of the zygomatic arch
Middle energizer point CA-3	The middle point of the connecting line between the upper and lower energizer acupoints
Lower energizer point CA-4	Inner side of the anterior margin of the mandibular angle
Ankle point CA-15	1/3 proximity of the connecting line between the knee and Chengjiang points
Foot point CA-16	0.5 inch lateral to the Chengjiang point
Note: The main acupoints used in the present study for pain relief. Abbreviations: CA, cheek acupuncture.	

The needles were removed after 30 minutes of needle retention, followed by compressing the needle hole with a cotton ball for a few minutes. After the needles were inserted, the analgesic effect was reevaluated through physical examination. If the pain was not fully relieved or only partially eased, the depth and direction of needle insertion were adjusted until significant or complete relief was achieved. During the 2-hour observation period, the CA group must not receive any other treatments. After 2 hours, if the patient remains dissatisfied with the analgesic effect, other pharmacological or non-pharmacological therapies may be administered based on the actual situation.

Etoricoxib group

120 mg EC tablets (Merck Sharp & Dohme Australia Pty Ltd) were distributed to participants to be taken in the clinic. Participants were required to take the tablets under supervision with a full 250 ml glass of water. A strict fasting period is required for 2 hours following administration.

Statistical methods

Statistical analyses were conducted using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). The measurement data were assessed for normal distribution using the Kolmogorov–Smirnov test and tested for homogeneity of variances using the Levene test. Normally distributed continuous data were presented as mean±standard deviation, while non-normally distributed data were expressed as median (25th-75th percentile). Categorical variables were expressed as number (%) .

Metric and ordinal data were analyzed using Student’s t-test or the Mann–Whitney U test, categorical data using the Chi-square test. Comparisons between groups at multiple time points were made using Linear Mixed Models. All statistical tests were taken as two-sided tests, and *P*-values less than or equal to 0.05 were considered statistically significant for the differences tested.

Results

The flow chart of this study is shown in Fig. 2. From September 2023 to December 2024, individuals were recruited from the Guangdong Provincial Hospital of Chinese Medicine. 136 individuals participated in the recruitment. Some of the participants did not meet the inclusion criteria (n = 32), while others refused to participate (n = 28). Finally, 76 individuals were eligible.

Characteristics of the included individuals

Table 2 shows the baseline characteristics of the 76 study participants included in the pilot trial with no significant differences in these variables.

Table 2
Baseline characteristics of the study participants.

	EC	CA	P value
	(n = 38)	(n = 38)	
Demographic characteristics			
Age (Year, ±s)	47.37 ± 8.49	47.29 ± 9.91	0.97
Gender (n; %)			
male	35(92.1)	36(94.7)	0.65
female	3(7.9)	2(5.3)	
Education (Years) (n; %)			
≤ 9	3(7.8)	2(5.3)	0.78
10–12	6(15.8)	6(15.8)	
13–15	27(71.1)	28(73.6)	
>15	2(5.3)	2(5.3)	
Clinical characteristics			
Duration of gout [Month, median(Q1,Q3)]	63(24,112)	51(13,102)	0.81
<12 (n; %)	7(18.4)	6(15.8)	0.80
13–36 (n; %)	10(26.3)	13(34.2)	
>36 (n; %)	21(55.3)	19(50.0)	
Duration of this gout attack [Hour, median(Q1,Q3)]	28(18,36)	28(12,36)	0.91
<12 (n; %)	8(21.1)	5(13.2)	0.94
12–24 (n; %)	6(15.8)	10(26.3)	
>24 (n; %)	24(63.1)	23(60.5)	
Uric acid-lowering medications			
Keep taking (n; %)	12(31.6)	17(44.7)	0.35
Never (n; %)	26(68.4%)	21(55.3)	
Note: Abbreviations: EC, etoricoxib; CA, cheek acupuncture.			

VAS analysis

Table 3 shows the results of VAS for the two groups at the various measurement time points. There was no statistically significant difference in VAS scores between the two groups prior to treatment ($P > 0.05$). The

variances between groups were significant at each time point from 0 mins after treatment to 2 h after treatment ($P < 0.05$). 2 h after treatment, the VAS score was 6 (5, 7) in the EC group and 2 (3, 4) in the CA group, with a statistically significant difference between the two groups ($p < 0.001$). A linear mixed-effects model was used to analyze changes in VAS scores over time across the two groups. Results indicated a statistically significant interaction effect between group and time ($p < 0.001$), suggesting differing trends in pain score changes between the two groups. As shown in Fig. 3, following intervention, the VAS scores in the CA group decreased rapidly, dropping to 4 (4, 5) at 0 minutes post-treatment and reaching a minimum of 2 (2.5, 3) at 1 hour, however, there was a mild increase in the VAS score to 2 (3, 4) at the 2-hour time point. In the EC group, the VAS score only began to decrease at 1 hour post-treatment, dropping to 6 (6, 8), and was followed by a further decrease to 6 (5, 7) at the 2-hour mark.

Table 3
Comparisons of VAS between CA and EC.

Outcome measure	Time	EC (n = 38)	CA (n = 38)	Z	P value	Linear mixed-effect model results (P value ^b)		
						Time	Group	Time×Group
VAS[median(Q1,Q3)]	Baseline	6 (6, 8)	7 (6, 8)	-0.47	0.63	<0.001	0.013	<0.001
	0 mins after treatment	6 (6, 8)	4 (4, 5)	-6.46	<0.001			
	30 mins after treatment	6 (6, 8)	2 (3, 3)	-7.38	<0.001			
	1 h after treatment	6 (6, 8)	2 (2.5, 3)	-7.35	<0.001			
	2 h after treatment	6 (5, 7)/	2 (3, 4)/	-6.58	<0.001			

Note: . $P < 0.05$ vs Baseline; $P < 0.05$ vs 1h. Abbreviations: CI, confidence interval; EC, etoricoxib; CA, cheek acupuncture; VAS, Visual Analogue Scale.

We also compared the pain level of VAS between the two groups, as shown in Table 4. At baseline, there were 20 participants suffering medium pain and 18 suffering severe pain in group EC, while in group CA 17 were medium and 21 were severe ($P > 0.05$). At 2h after treatment, there were 2 suffering light pain, 26 medium pain, and 10 severe pain in group EC, while in group CA, 26 light pain and 12 medium pain, the difference of change in pain level between group EC and group CA was significant ($P < 0.00$).

Table 4
Comparisons of pain level between CA and EC.

Outcome measure	Time		EC (n = 38)	CA (n = 38)	Z	P value
VAS - Pain level (n; %)	Baseline	Mild (n; %)	0(0)	0(0)	-0.68	0.49
		Medium (n; %)	20(52.6)	17(44.7)		
		Severe (n; %)	18(47.4)	21(55.3)		
	0 mins after treatment	Mild (n; %)	0(0)	5(13.2)	-4.46	<0.001
		Medium (n; %)	20(52.6)	31(81.6)		
		Severe (n; %)	18(47.4)	2(5.2)		
	30 mins after treatment	Mild (n; %)	0(0)	31(81.5)	-7.20	<0.001
		Medium (n; %)	22(57.9)	7(18.5)		
		Severe (n; %)	16(42.1)	0(0)		
	1 h after treatment	Mild (n; %)	0(0)	31(81.6)	-7.11	<0.001
		Medium (n; %)	28(73.7)	7(18.4)		
		Severe (n; %)	10(26.3)	0(0)		
	2 h after treatment	Mild (n; %)	2(5.3)	26(68.4)	-5.91	<0.001
		Medium (n; %)	26(68.4)	12(31.6)		
		Severe (n; %)	10(26.3)	0(0)		

Note: Abbreviations: EC, etoricoxib; CA, cheek acupuncture; VAS, Visual Analogue Scale.

Joint tenderness

As shown in Table 5, at baseline, there were 28 participants suffering fairly tender and 10 suffering very tender in group EC, while in group CA 22 were fairly tender and 16 very tender ($P > 0.05$). After 2h treatment, there was 1 participant suffering slightly tender, 28 fairly tender, and 9 very tender in group EC, while in group 34 CA slightly tender, 3 fairly tender, and 1 very tender ($P < 0.00$).

Table 5
Comparisons of joint tenderness between CA and EC.

Outcome measure	Time		EC (n = 38)	CA (n = 38)	Z	P value
joint tenderness (n; %)	Baseline	Not tender(n; %)	0 (0)	0 (0)	-1.441	0.15
		Slightly tender(n; %)	0 (0)	0 (0)		
		Fairly tender(n; %)	28 (73.7)	22 (57.9)		
		Very tender(n; %)	10 (26.3)	16 (42.1)		
		Extremely tender(n; %)	0 (0)	0 (0)		
	2h after treatment	Not tender(n; %)	0 (0)	0 (0)	-7.134	<0.00
		Slightly tender(n; %)	1 (2.6%)	34 (89.5)		
		Fairly tender(n; %)	28 (73.7)	3 (7.9)		
		Very tender(n; %)	9 (23.7)	1 (2.6)		
		Extremely tender(n; %)	0 (0)	0 (0)		

Note:. Abbreviations: EC, etoricoxib; CA, cheek acupuncture.

Patient feedback

Table 6 shows patient feedback of the 76 study participants included in the pilot trial with a significant difference ($P < 0.00$). After 2h treatment, 29 participants felt somewhat improved and 9 felt unchanged in group EC, while in group CA 23 felt very much improved, 11 much improved, 2 somewhat improved, and 2 unchanged ($P < 0.00$).

Table 6
Comparison of patient's feedback between CA and EC.

Outcome measure	Time		EC (n = 38)	CA (n = 38)	Z	P value
patient's feedback(n; %)	2h after treatment	Completely disappeared (n; %)	0 (0)	0 (0)	-6.861	<0.001
		Very much improved (n; %)	0 (0)	23 (60.5)		
		Much improved (n; %)	0 (0)	11 (28.9)		
		Somewhat improved (n; %)	29 (76.3)	2 (5.3)		
		Unchanged (n; %)	9 (23.7)	2 (5.3)		
		Slightly worse (n; %)	0 (0)	0 (0)		
		Much worse (n; %)	0 (0)	0 (0)		
		Very much worse (n; %)	0 (0)	0 (0)		
Note:. Abbreviations: EC, etoricoxib; CA, cheek acupuncture.						

Adverse events

There were 2 adverse events that occurred in group EC during the trial, one patient felt dizziness, and another felt nauseous after taking EC. No adverse events were observed during the trial in group CA.

Discussion

This study was a randomized controlled trial for adults with AGF, comparing CA with EC. The mean value in VAS was high at baseline, and most patients suffered from moderate to high pain. More than 90% of the subjects were male, which is consistent with the gender-specific nature of gout. This study assessed the immediate effectiveness of a single session, whereby subjects received a single on-site treatment and were observed for two hours. This resulted in a complete absence of shedding in all cases.

CA therapy demonstrated a statistically significant reduction in foot pain and joint tenderness relative to the baseline in 2-hour follow-ups. The dynamic VAS change curves demonstrated that the application of acupuncture to the cheek provided superior pain relief in comparison to EC at each designated time point. Additionally, the onset of action was observed to be exceptionally rapid, occurring immediately following the administration of the needle. Compared to EC, CA has significant advantages in terms of both pain reduction and time to onset of analgesic effect, thus making the subject's outpatient experience more satisfying.

However, a transient rebound in the VAS score was observed in the CA group between 1 and 2 hours post-treatment. This phenomenon is consistent with the characteristic gradual decline of the residual acupuncture effect following needle removal after a 30-minute session, which underscores the rationale for maintaining a regular treatment frequency (e.g., once daily or every three days) in clinical practice. As the present study was specifically designed to assess the immediate 2-hour analgesic effect, follow-up beyond this period was not conducted. Further studies are warranted to determine the duration of the analgesic effect of cheek acupuncture for gout, which is crucial for establishing its optimal treatment frequency.

The key to AGF treatment is the rapid and effective control of the acute inflammatory response. Guidelines recommend the use of NSAIDs, colchicine, and corticosteroids, either individually or in combination^[18]. Adrenocorticotrophic hormone and anti-IF-1 β medications also can be administered to alleviate the severe pain associated with AGF^[19, 20]. These medications generally require a certain time to provide pain relief. According to Cheng's research, the onset of pain relief for rofecoxib, and meloxicam occurs within 30 minutes to an hour after the first dose^[21]. In this study, VAS in the EC group began to decline since 1 h after treatment, the immediate pain relief was similar to meloxicam. In a multi-center, double-blind study, patients with acute gout reported a 1-cm reduction in VAS after 2 hours of oral prednisolone administration^[22]. Oral colchicine has the slowest onset of action, typically providing pain relief about 24 hours after taking the first dose^[23]. The above study suggests that oral pain medications vary in their onset of action, with patients having to wait for half an hour or more for the medication to take effect. If the patient has to pay a fee and wait to pick up the medication, it takes even longer time for the pain relief to begin. Therefore, for immediate pain relief, cheek acupuncture demonstrates a clear advantage in its rapid onset compared to oral medication.

In addition to medication, localized ice packs, acupuncture and the topical application of traditional Chinese medicine can be used to relieve AGF symptoms^[24–27]. CA, a micro-needle therapy developed by Professor Wang Yongzhou, is characterized by painlessness, standardization, simplicity, and precision^[28]. Rooted in the theories of Da San Jiao, bioholography, and physical/mental integration, CA addresses various diseases by stimulating corresponding parts of the body through specific points on the cheeks^[29, 30]. Clinical studies have demonstrated the significant effect of CA in treating painful conditions, particularly in managing acute pain episodes and postoperative pain^[31]. In our study, CA led to a notable reduction in pain within two hours, with a more pronounced decrease in VAS scores. The onset of action was extremely rapid, occurring immediately after needle administration, suggesting that CA provides faster and more effective pain relief compared to the onset and efficacy of drugs reported in existing literature.

CA employs the acupoint holographic law, derived from bioholography theory, to treat acute pain^[32]. This method involves a series of facial points, extending from the angle of the jaw down to the chin, which correspond to the lower extremities of the body^[33]. In our study, we selected points (CA-15 and CA-16) corresponding to the ankle and toe joints, areas that are particularly susceptible to acute gout. The Da San Jiao theory is a cornerstone of Chinese medicine, positing that the San Jiao regulates and integrates the functions of the entire body, overseeing life activities holistically^[15]. In treating patients with AGF, we utilized the upper energizer point (CA-2), middle energizer point (CA-3), and lower energizer point (CA-4) to

enhance visceral functions and promote the circulation of qi and blood, facilitating more rapid pain relief. Additionally, stimulating the head point (CA-1) helps address stress responses associated with psychological factors, thereby facilitating an integrated mind-body treatment that enhances overall pain management.

The precise mechanism by which CA reduces pain remains unclear. It is possible that CA may activate the body's opioid peptide system, thereby releasing substances such as endorphins which produce analgesic effects^[30]. By stimulating the release of neurotransmitters such as endogenous opioid peptides, serotonin, and norepinephrine, CA is capable of reducing the sensitivity of peripheral spinal cord injury receptors, thereby mediating sustained pain relief^[34–38]. It has been postulated that the application of acupuncture to the cheeks modulates pain perception at the central nervous system level, by stimulating specific facial acupuncture points that influence the transmission and processing of pain signals^[39]. Additionally, CA has been observed to influence the immune system, with a reduction in pain by lowering the concentration of inflammatory factors and mitigating the inflammatory stress response^[40].

Despite the efficacy of medications in treating AGF, there is growing concern about their potential gastrointestinal, renal, and cardiovascular side effects^[41]. Patient feedback is a crucial indicator of treatment effectiveness. In this study, patients expressed high satisfaction with CA, likely due to the rapid pain relief and fewer side effects. Feedback also suggested that CA improved the quality of life and daily activities. This underscores the potential value of CA in the acute management of gout and offers valuable insights for future clinical practice and research.

The findings from this study may provide scientific evidence for physiotherapists to apply CA to treat patients with AGF. This is the first randomized controlled study to observe the pattern of oral pain medication and acupuncture pain relief effects over time. Research reveals that immediate outpatient intervention with CA can provide patients with pain relief in the shortest possible time. This study may enlighten further studies in the development of pain management in other painful conditions.

Our pilot study has several limitations. Firstly, the design included a sham acupuncture control arm, the placebo effect of acupuncture cannot yet be evaluated. Secondly, it was not a double-blind clinical trial, so the investigator administering the treatment was aware of the subgroup of subjects. This study needed to record VAS before treatment, 0 min, 30 min, 1 h, and 2 h after the start of treatment, so evaluators inevitably known the grouping of subjects. Both of the above factors can lead to bias. Finally, this is a small clinical trial and larger sample size studies are needed to further evaluate the efficacy of CA.

Conclusions

To conclude, CA provides quick pain relief for gout sufferers. Compared to oral pain medication, it effectively eliminates the time lag between consultation and the medication's onset of action, thus exhibiting a more significant advantage in improving the satisfaction of the consultation.

Abbreviations

AGF	Acute gouty flare
CA	Cheek acupuncture
EC	Etoricoxib
VAS	Visual Analogue Scoring
NSAID	Nonsteroidal anti-inflammatory drug
KUMCR	Key Unit of Methodology in Clinical Research

Declarations

Acknowledgments

This trial was funded by the Guangdong Provincial Hospital of Chinese Medicine. We gratefully thank the patients taking part in this trial and all the investigators involved.

Authors' contribution

YPL and GJF conceived the trial and are its chief and deputy chief investigators, respectively. GJF, YPL, and ZJY contributed to the study design. YPL, GJF, ZJY, SL and YHL were involved in the conduct of the trial and data collection. YHL was responsible for the preparation for randomization and allocation. YPL and SL developed the statistical analysis plan and conducted the analyses, with input from ZJY, QYL and YHL. ZJY and YPL wrote the first draft of the manuscript and all authors provided input into revising and finalizing the report.

Funding

This trial was funded by the Yongzhou Wang Academic Experience Inheritance Workshop Support Program from Guangdong Provincial Hospital of Chinese Medicine (No.2021-06), Fundamental and Applied Basic Research Program of Guangdong Province (2023A1515220052), Guangdong Provincial Medical Science (2022A1515220069, A2024563) and Technology Research Fund Project and Scientific and Technological Research Specialization program from Guangdong Provincial Hospital of Chinese Medicine (No.YN2023MS24/ YN2022QN17).

Availability of data and materials

Individual participant data will not be made available to the public, but might, in a de-identified form, be accessible for future collaborative purposes after approval of a proposal and a signed data access agreement. The study protocol can be obtained from the corresponding author by email.

Ethics approval and consent to participate

This trial was approved by the Ethics Committees of Guangdong Provincial Hospital of Chinese Medicine and preregistered at Clinicaltrials.gov (Clinical trial number: NCT06001112) on 21 August 2023. Every

participant was informed of the purpose of the trial with possible risks and signed an informed consent document.

Competing interest

The authors declare that they have no competing interests.

References

1. Punzi L, Scanu A, Galozzi P, et al. One year in review 2020: gout. *Clin Exp Rheumatol*. 2020;38:807–21.
2. Martins D, Tonon CR, Pacca RL, et al. Gout Storm. *Am J Case Rep*. 2021;22:e932683.
3. GBD 2021 Gout Collaborators. Global, regional, and national burden of gout, 1990–2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. *Lancet Rheumatol*. 2024;6:e507–17.
4. Yu K-H, Chen D-Y, Chen J-H, et al. Management of gout and hyperuricemia: Multidisciplinary consensus in Taiwan. *Int J Rheum Dis*. 2018;21:772–87.
5. N D, Tr M, Lk S. Gout. *Lancet Lond Engl*. 2016;388.
6. Wj T, J F, Tl J, et al. Study for Updated Gout Classification Criteria: Identification of Features to Classify Gout. *Arthritis Care Res*. 2015;67.
7. Perez-Ruiz F, Dalbeth N. Gout. *Rheum Dis Clin North Am*. 2019;45:583–91.
8. American Pain Society Quality of Care Committee. Quality improvement guidelines for the treatment of acute pain and cancer pain. *JAMA*. 1995;274:1874–80.
9. Stewart S, Guillen AG, Taylor WJ, et al. The experience of a gout flare: a meta-synthesis of qualitative studies. *Semin Arthritis Rheum*. 2020;50:805–11.
10. Clebak KT, Morrison A, Croad JR. Gout: Rapid Evidence Review. *Am Fam Physician*. 2020;102:533–8.
11. McKenzie BJ, Wechalekar MD, Johnston RV, et al, Buchbinder R. Colchicine for acute gout. *Cochrane Database Syst Rev*. 2021;8:CD006190.
12. Li S-H, Hu W-S, Wu Q-F, et al. The efficacy of bloodletting therapy in patients with acute gouty arthritis: A systematic review and meta-analysis. *Complement Ther Clin Pract*. 2022;46:101503.
13. Jh H, A S, Hs S. Systematic Review and Meta-Analysis of Efficacy and Safety of Fire Needling and Warm Needling on Acute Gout. *J Pharmacopuncture*. 2022;25.
14. Lee G, Cho FY, Goo B, et al. Acupuncture for gouty arthritis: A PRISMA-compliant protocol for a systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2020;99:e23527.
15. Wang YZ. *Cheeks Acupuncture Therapy*. Beijing, China: People's Health Publishing House Co. Ltd; 2017.
16. LIU Rongrong, YANG Honghong, LU Hongxiu. Research progress on the analgesic mechanism of buccal needle and its application to postoperative pain. *China Med Her*. 2022;19:53–6.

17. Issa LM, Thybo KH, Hägi-Pedersen D, et al. Participants with mild, moderate, or severe pain following total hip arthroplasty. A sub-study of the PANSALD trial on paracetamol and ibuprofen for postoperative pain treatment. *Scand J Pain*. 2021;21(2):384–392.
18. Dalbeth N, Choi HK, Joosten LAB, et al. Gout. *Nat Rev Dis Primer*. 2019;5:69.
19. Ct T, Nc B, Kw K. Corticotropin for acute management of gout. *Ann Pharmacother*. 2001;35.
20. Mh P, Bf M. Therapeutic approaches in the treatment of gout. *Semin Arthritis Rheum*. 2020;50.
21. Cheng T-T, Lai H-M, Chiu C-K, et al. A single-blind, randomized, controlled trial to assess the efficacy and tolerability of rofecoxib, diclofenac sodium, and meloxicam in patients with acute gouty arthritis. *Clin Ther*. 2004;26:399–406.
22. Rainer TH, Cheng CH, Janssens HJEM, et al. Oral Prednisolone in the Treatment of Acute Gout: A Pragmatic, Multicenter, Double-Blind, Randomized Trial. *Ann Intern Med*. 2016;164:464–71.
23. Schlesinger N. Management of acute and chronic gouty arthritis: present state-of-the-art. *Drugs*. 2004;64:2399–416.
24. Ni Z, Xiao Q, Xia Z, Kuang K, Yin B, Peng D. Electroacupuncture for acute gouty arthritis: a systematic review and meta-analysis of randomized controlled trials. *Front Immunol*. 2023;14:1295154.
25. Wang S, Liu W, Wei B, Wang A, Wang Y, Wang W, et al. Traditional herbal medicine: Therapeutic potential in acute gouty arthritis. *J Ethnopharmacol*. 2024;330:118182.
26. Wb L, Sh W, Bi M, Sh C. Acupuncture for gouty arthritis: a concise report of a systematic and meta-analysis approach. *Rheumatol Oxf Engl*. 2013;52.
27. Lu C-X, Deng X-J, Chen M, Xiao C-H, Cui J. Different stimulation methods on auricular points for primary dysmenorrhea: a randomized controlled trial. *Zhongguo Zhen Jiu Chin Acupunct Moxibustion*. 2021;41:737–41.
28. Liu M, Peng G. Observation on the effect of buccal needling combined with acupoint injection for the treatment of hearing impairment after chemoradiotherapy for nasopharyngeal carcinoma. *J Guangzhou Univ Tradit Chin Med*. 2022;39:2602–6.
29. Wu C, Duan Y, Zhang Z. Efficacy observation of buccal acupuncture combined with danhong injection for cardiac syndrome X. *Shanghai J Acumox*. 2022;41:868–72.
30. Jie W, Fang X, Pu R, Su C, Zhang Y, Pu Y, et al. Analgesic effect of buccal acupuncture on acute arthritis in rabbits and underlying mechanisms. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. 2017;42:517–21.
31. Fan X. Theories and Clinical Application of Buccal Acupuncture. *Chin J Nat Med*. 2007;;29–33.
32. Xt Z, Yq Z, Wh Z. ZHANG Wei-hua's experience in clinical treatment of somatalgia with "point-zone-strip stimulation technique" of acupuncture. *Zhongguo Zhen Jiu Chin Acupunct Moxibustion*. 2022;42.
33. Huang S, Huang Y, Li X, Wang S, Zhuo Y. Overview of Cheek Acupuncture Therapy and Its Clinical Application. *J Clin Acupunct Moxibustion*. 2017;33:72–5.
34. Yao C, Zhang Y, Lu P, Xiao B, Sun P, Tao J, et al. Exploring the bidirectional relationship between pain and mental disorders: a comprehensive Mendelian randomization study. *J Headache Pain*. 2023;24:82.
35. Han J-S. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci*. 2003;26:17–22.

36. Sprouse-Blum AS, Smith G, Sugai D, Parsa FD. Understanding endorphins and their importance in pain management. *Hawaii Med J.* 2010;69:70–1.
37. Zhang R, Lao L, Ren K, Berman BM. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology.* 2014;120:482–503.
38. Sun Y, Zhou Q, Xiao J, Cheng Z. The effect of buccal acupuncture on the postoperative visceral pain in patients undergone gynecological laparoscopic surgery and its action mechanism. *Jiangxi Med.* 2022;57:584–6.
39. Wang Y, Yang L, Wu Y. Case report: Cheek acupuncture exhibits an immediate effect in relieving severe pain associated with nerve compression or damage of central nervous system and its potential mechanism of action. *Front Neurosci.* 2023;17:1211361.
40. Zhou Y, Zhu M, Hu H, Niu C, Yang X, Zhang J, et al. Effect of buccal needle therapy on perioperative analgesic effects in patients undergoing laparoscopic radical colon cancer surgery. *J Clin Anesthesiol.* 2024;40:704–8.
41. Js B, Ls S. Cardiovascular and gastrointestinal effects of COX-2 inhibitors and NSAIDs: achieving a balance. *Arthritis Res Ther.* 2005;7 Suppl 4 Suppl 4.

Figures

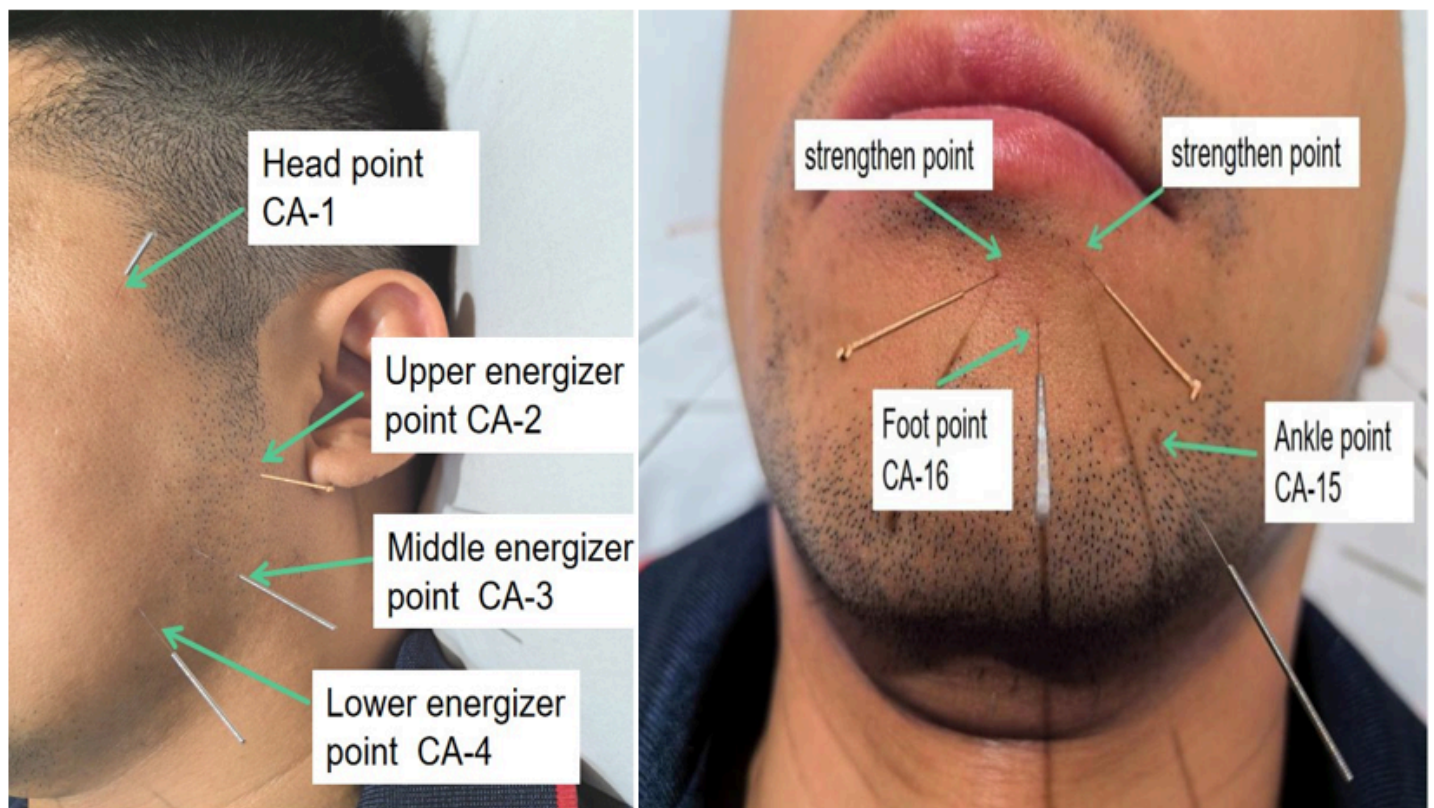


Figure 1

Cheek acupuncture illustration

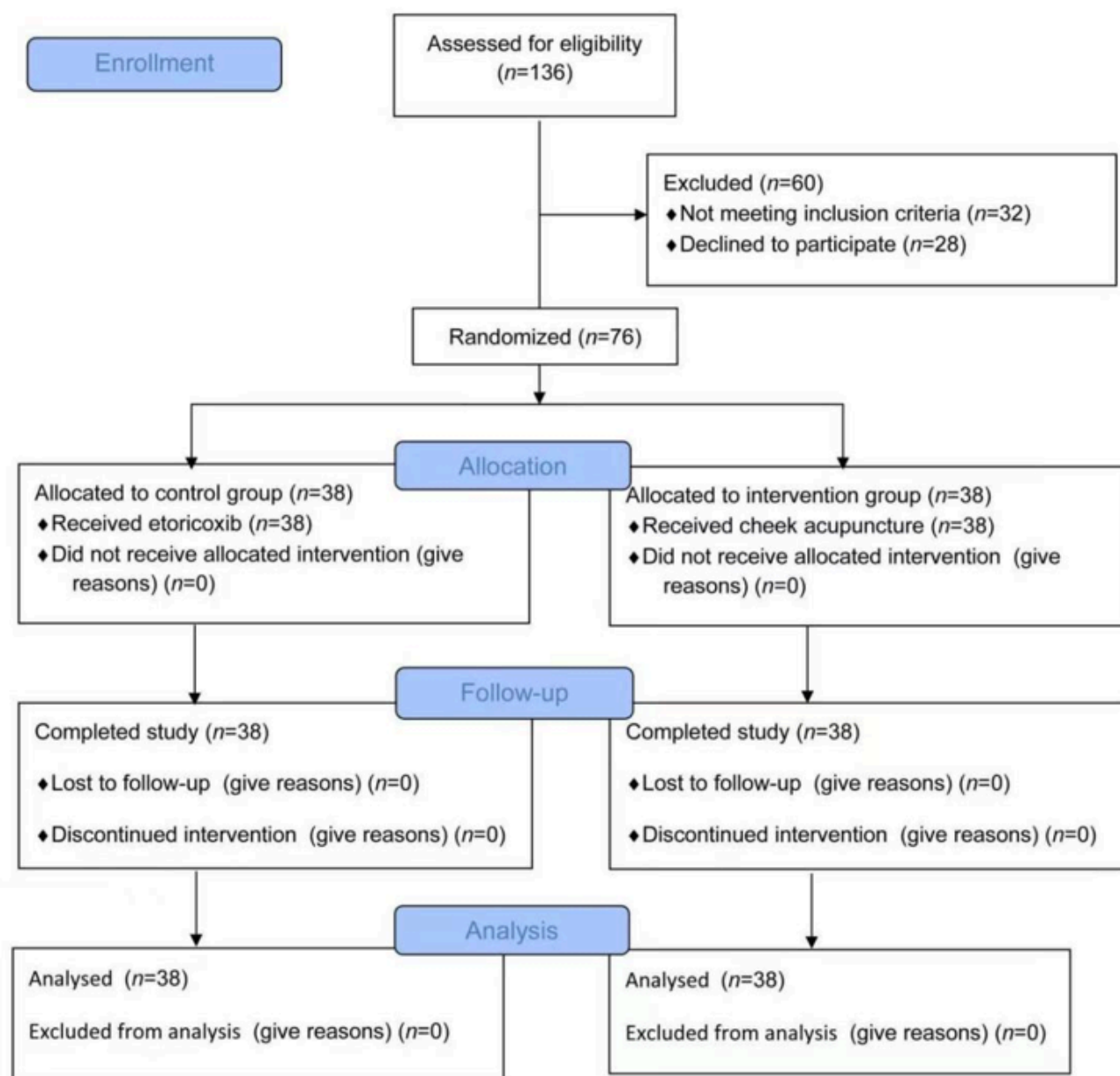


Figure 2

Flow Chart of Enrolled Patients

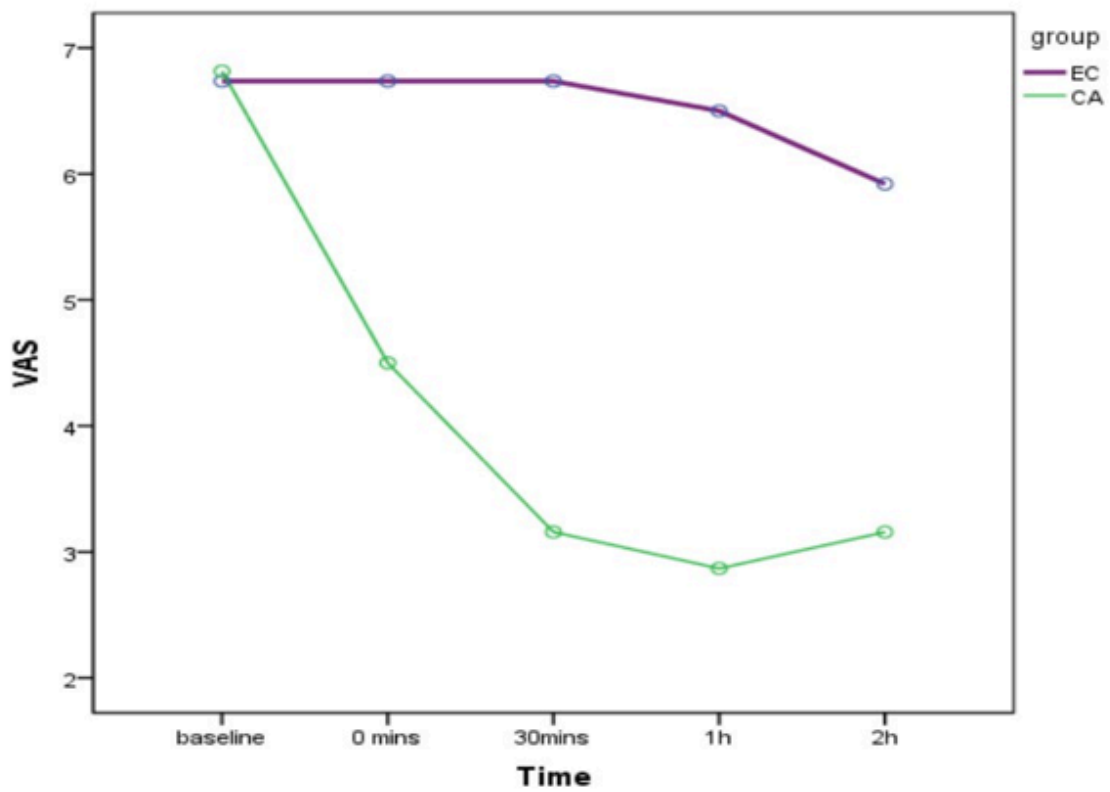


Figure 3

Dynamic VAS change curves of two groups

Note: Abbreviations: VAS, Visual Analogue Scale.