Received: 14 November 2019 | Revised: 31 January 2020 | Accepted: 15 February 2020

DOI: 10.1111/joor.12952

ORIGINAL ARTICLE

JOURNAL OF ORAL REHABILITATION WILEY

Comparison of acupuncture on specific and non-specific points for the treatment of painful temporomandibular disorders: A randomised controlled trial

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Abstract

Background and Objective: The aim of this single-centre, two-arm, parallel-group, double-blinded, randomised controlled trial was to investigate the disputed specific effectiveness of acupuncture by comparing acupuncture on specific and non-specific points among patients with non-chronic, painful TMDs.

Methods: Following predefined eligibility criteria, 49 consecutive patients of both sexes were recruited to the study. All subjects were diagnosed with a non-chronic (Graded Chronic Pain Scale grade <3) painful TMD, as assessed using the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). Patients were randomly assigned to group A (acupuncture on specific points) or group B (acupuncture on non-specific points) after the initial examination (T0). Both acupuncture treatment sessions were conducted by a trained dentist once a week for four weeks. The examination was repeated five weeks (T5) after T0 by one calibrated examiner who was unaware of the study groups. Characteristic pain intensity (CPI) was evaluated as the main outcome criterion and compared between times and treatment groups by means of non-parametric tests (significance level set at $P = .05$). Secondary outcomes comprised the maximum corrected active mouth-opening without pain (MAO); patients' expectations regarding acupuncture treatment and pain development; depressivity; and oral health-related quality of life (OHRQoL).

Results: A total of 41 patients (38 female) successfully completed the study (mean age: 40.17 ± 16.61). The two groups did not differ significantly at any time in terms of age and CPI. However, CPI was significantly ($P < .05$) lower at T5 than at T0 for both groups (29.66 and 30.35% lower in group A and group B, respectively). An increase in MAO was observed at T5 for both groups but was significant for group B only ($P = .016$). All patients had positive expectations of acupuncture therapy, and the two groups did not differ significantly at T5 with regard to the extent to which their

The peer review history for this article is available at https://publons.com/publon/10.1111/JOOR.12952/

Trial Registration: ClinicalTrials.gov-NCT02637544

expectations had been fulfilled by the treatment (P = .717). Comparison of T0 and T5 showed a statistically significant reduction of depressivity for group A (P = .0205), but no significant change for group B (P = .329). At T5, OHRQoL had improved significantly for both groups (group A, P = .018; group B, P < .001) compared with at T0. **Conclusions:** Acupuncture on both specific and non-specific points reduces the non-dysfunctional pain of TMD patients. The effect of acupuncture on painful TMD cannot be attributed to the specific point selection.

KEYWORDS

acupuncture, effectiveness, oro-facial pain, randomised controlled trial, temporomandibular disorders

1 | BACKGROUND

Recent decades have seen a continuous improvement in diagnostic protocols for temporomandibular disorders (TMDs).[1,2] However, the development of evidence-based treatment options for painful TMDs has not kept pace. This might partly be because the available treatments and/or their combinations are largely sufficient for the management of painful TMDs.[3] The most common treatment options for pain-related TMDs are occlusal splint therapy; pharmacological interventions (including analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), as well as local anaesthetics when trigger points are present); muscle relaxants; antidepressants; physical therapy; and behavioural and self-management therapies.[4-8]

A well-known ancillary method to the primary therapy methods mentioned above is acupuncture, a component of traditional Chinese medicine (TCM). TCM is an independent, ancient medical concept developed in China over a period of 3000 years.[9] According to TCM, the body contains the meridian system, also called the channel network, which is a path through which the life energy "qi" flows. The practice of acupuncture consists of inserting thin needles into the skin and muscles on specific acupuncture points located along the meridians, for the treatment of a variety of conditions. In addition to traditional manual acupuncture, other methods are also used to stimulate acupuncture points for therapeutic purposes, for example electroacupuncture, acupressure, laser acupuncture and moxibustion. In addition to acupuncture, TCM includes other approaches such as herbal medicine, traditional massage (tui na) and meditation (qi gong). The more common use of acupuncture as opposed to other TCM options seems to be based on its greater practicability. In TCM diagnosis, the disorders, pain or dysfunctionality of an organ system are associated with the meridians. Possible curative responses can then be stimulated by means of the acupuncture points on the TCM diagnosis-related meridian paths.[10]

One of the first reports on acupuncture in modern Western clinical therapy was published in 1950 by Rott.[11] Controlled clinical trials studying the effectiveness of acupuncture employ different control groups, such as non-penetrating needle or penetrating needle in a non-specific point outside the main meridians.[12] A recent meta-analysis showed that acupuncture was superior to both sham acupuncture and no acupuncture control for the following chronic pain conditions: non-specific musculoskeletal pain, osteoarthritis, chronic headaches, shoulder pain and non-specific low back pain.[13]

A World Health Organization (WHO) report listed TMDs among the 28 diseases, symptoms and conditions that have been effectively treated by the use of acupuncture.[14] This report was based mainly on a pioneering systematic review[15] and early clinical studies.[16,17] However, more recent systematic reviews showed that the evidence for acupuncture as a symptomatic treatment for TMDs with the use of sham acupuncture as a control is limited.[18] Yet although scientific evidence of its efficacy is weak, acupuncture treatment does appear to relieve the signs and symptoms of pain among myofascial TMD patients when compared with splints/no treatment, sham acupuncture and placebo laser acupuncture as controls.[19] In addition, specific acupuncture therapy is effective at reducing the degree of pain among patients with TMDs, especially those with myofascial pain symptoms, compared with both sham non-penetrating acupuncture and sham laser therapy.[12]

The main limitations of the clinical trials studied might have resulted from an unclear diagnosis of TMDs due to a lack of reliable, standardised diagnostic tools; a lack of differentiation between patients with chronic (ie dysfunctional) and persistent/non-chronic TMD pain; a non-standardised selection of acupuncture treatment points; and the use of different (skin-penetrating or non-penetrating) controls. Furthermore, acupuncture was often used for patients with treatment-resistant painful TMDs, thus representing a treatment of last resort.[20] No clear data are yet available on the possible specific effectiveness of acupuncture as a first-line treatment for patients with non-chronic painful TMDs.

The primary objective of our randomised, double-blind, controlled clinical trial was to investigate the specific effect of acupuncture on the course of pain for patients with non-chronic (ie non-dysfunctional) painful TMDs of myogenous and/or arthrogenous origin. We also analysed the maximum active mouth-opening and treatment expectations of the patients, as well as other patient-reported outcome measures such as depressivity and quality of life. Our study hypothesis was that specific acupuncture treatment

is significantly more effective at reducing TMD pain than non-specific needle penetration.

2 | METHODS

The reporting in this single-centre two-arm parallel-group double-blinded randomised controlled trial adheres to the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA).[21]

2.1 | Ethical approval

The study protocol was approved by the ethics committee of the Medical Faculty of Heidelberg University (approval no.: S-099/2014), and the trial was registered on ClinicalTrials.gov (NCT02637544). The study conformed to the Declaration of Helsinki and was performed according to the European Medicines Agency Guidelines for Good Clinical Practice. Before participation, all patients or their parents/ legal guardians received oral and written study information and signed a written consent form.

2.2 | Study sample

The authors of this study recruited participants from among consecutive patients seeking treatment for non-odontogenic oro-facial pain at the Department of Prosthodontics of the University Clinic of Heidelberg between May 2014 and April 2016. Eligible participants were selected in accordance with pre-set criteria. The study included adult patients of both sexes who were seeking treatment for painful, non-chronic (ie non-dysfunctional), TMD-related pain, as diagnosed by one calibrated examiner using the German version of the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). Only patients with pain of myogenous and/or arthrogenous origin were enrolled in the study. The Graded Chronic Pain Scale (GCPS, version 1.0)[22] was used to grade pain status in the screening phase. Patients with a GCPS score of 1 or 2 were eligible for the study.

Patients were excluded from the study if they had chronic (ie dysfunctional) facial pain (GCPS score of 3 or 4); facial pain of dental, systemic (eg rheumatoid arthritis), traumatic (facial trauma or surgery) or neuropathic origin; were in need of dental treatment; or were insufficiently fluent in the German language. Other exclusion criteria were pregnancy, regular use of sedative drugs, drug or alcohol abuse, and needle phobia.

Forty-nine patients (of whom three were male) who satisfied all eligibility criteria received oral and written study information and signed a written informed consent form before the start of the study.

The same calibrated examiner used the DC/TMD to examine all patients before their allocation to a study subgroup. All patients diagnosed with TMD pain received information on the disease and its multifactorial aetiology, and they were advised to avoid extreme movements of the jaw (eg yawning) and chewing hard food and chewing gum, according to a standard text developed in advance. Each study participant was randomly assigned to one of two treatment groups: A or B. This allocation was performed on the basis of a standard randomisation protocol (block randomisation with four patients in each group) developed by a person not connected to the study (external randomisation centre), in which numbered, sealed, non-transparent envelopes containing the allocation data were opened sequentially after the DC/TMD examination. Group A patients received acupuncture treatment on specific points, whereas group B patients received acupuncture treatment on non-specific points. To control for the expectations of the patients and the placebo effect of the treatment, the verbal cues used to explain the intervention and the prognosis were also standardised (Figure 1).

2.3 | Study protocol

The acupuncture sessions were repeated once a week for four consecutive weeks (T1-T4). One week after the fourth acupuncture session, the same calibrated examiner (who was still unaware of the group allocations) used the DC/TMD to examine all patients again (T5). If they wished to do so, patients who were still in pain after the active study period continued their treatment by means of acupuncture and/or other standard treatment protocols of the Department of Prosthodontics, such as a home exercise protocol and intraoral splints, until they were pain-free or ceased attending their regular appointments.

The study protocol is summarised in Figure 1. Before and after each acupuncture appointment, all patients completed standardised questionnaires regarding their pain status and treatment expectations. Their current, mean and worst pain intensity was rated on a numeric rating scale (NRS).

2.4 | Specific acupuncture treatment protocol (protocol A)

Patients allocated to group A were treated using a protocol of specific acupuncture points (Figure 2). These points were selected according to the principles of TCM and with regard to clinical studies included in previous review of Jung et al[18] and our pilot study on TMD diagnosis according to the "Heidelberg model" of TCM.[10] According to the TCM, no specific points exist for TMD pain, only points for general pain in the head.[12,23] However, based on our pilot study results, the most frequent TCM diagnosis for TMD pain patients is cardiac constitution with yin deficiency, which is related to the gall bladder (BL), stomach (ST), small intestine (SI) and triple energiser (TE) meridian systems. For this reason, we used five local (BL-2, BL-3, SI-19, ST-7 and TE-21) and two distal (BL-34 and SI-3) points on these meridians on each side of the body for the specific-point treatment group.

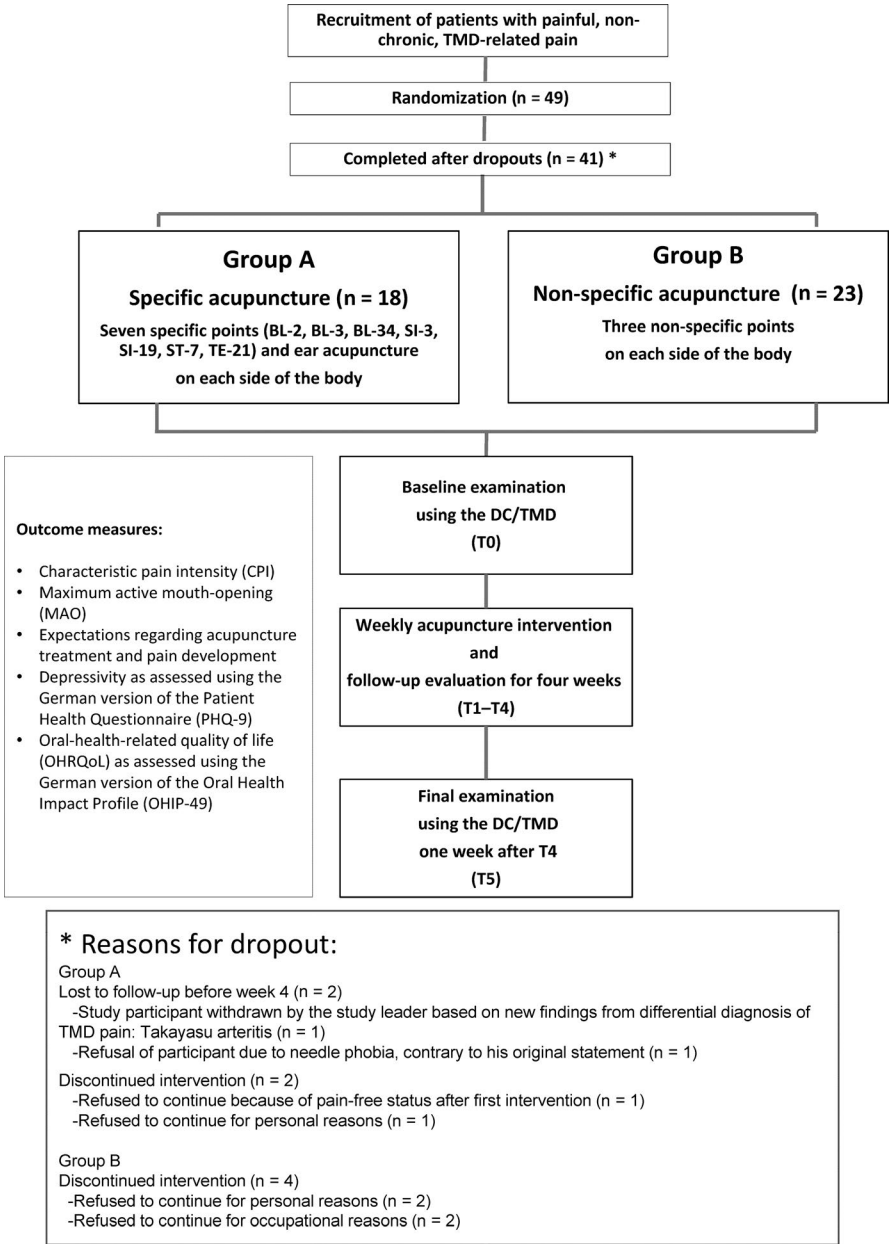

FIGURE 1 Flow chart of patients, intervention time points and outcome measures (based on CONSORT)

All acupuncture procedures were performed by the same dentist trained in TCM. Each acupuncture session lasted 45 minutes, during which time the patient was lying comfortably on a hospital bed. In total, 14 sterile, disposable needles (0.30 × 30 mm, Asiamed special, coated needles with copper loop handle; asia-med GmbH, Pullach, Germany) were used for each patient (seven on each side of the body). Each needle penetrated the skin to a depth of 1 cm, was kept in place for 45 minutes and was periodically (every 15 minutes) activated by means of an even clockwise and counterclockwise rotation by the patient in question. In addition, after the body acupuncture session, acupuncture was performed on both ears (on the lobule, indicated for treating disorders of the temporomandibular joint region) according to Chinese and Western Systems of ear acupuncture.[24,25] After locating the lobule, sterile and disposable intradermal needles (gold-plated, semi-permanent needle, Asiamed apex gold; asia-med GmbH, Pullach, Germany) were inserted into this area of both ears (Figure 2). The needles remained in place for the next seven days until the next acupuncture appointment. The patients were also instructed to stimulate the temporary ear needles with an accompanying magnet three times per day.

Before each follow-up session, patients were explicitly asked to report any unusual or uncomfortable effects they thought were attributable to the acupuncture treatment.

2.5 | Non-specific acupuncture treatment protocol (protocol B)

Patients allocated to group B received the same acupuncture protocol on both sides of the body at three pre-selected non-specific points. To avoid any interaction, these three points were selected to be as far away as possible from any meridians; they were therefore located

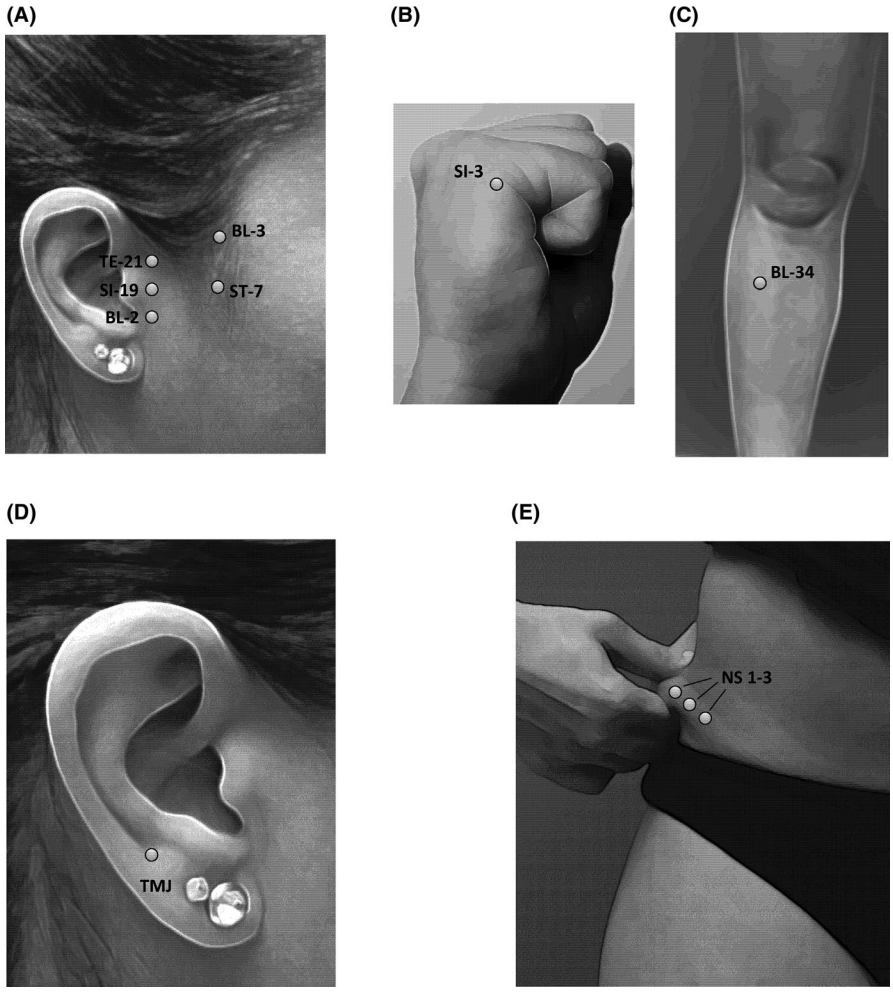

FIGURE 2 An overview of acupuncture intervention points: A–C, Traditional Chinese medicine (TCM)-specific acupuncture points for the treatment of pain related to temporomandibular disorders (TMDs). D, Ear acupuncture point related to temporomandibular joint pain according to Chinese and Western Systems of Ear Acupuncture. E, Non-specific acupuncture points with no connection to the meridians of TCM.

1 cm below the last rib at 1 cm intervals on the axillary line of the trunk, in the adipose tissue of the lateral waistline, as conducted previously by other researchers.[26] All non-specific acupuncture procedures were performed by the same person, using the same penetrating needles as those in the protocol A. The non-specific, penetrating needle acupuncture sessions had the same duration and took place in the same room and on the same hospital bed as the acupuncture intervention at specific points. In total, six acupuncture needles were used (three for each side of the body). The patients were asked to comment orally on their subjective feelings after the needle had been inserted, and the points had been stimulated by the needles. All participants in both groups confirmed they had experienced the feeling known as DeQi in TCM after the penetration of the skin and often described their feeling as "pricking," "numbness" or "spreading." The non-specific acupuncture points are listed and described in Figure 2. Patients in group B did not receive ear acupuncture. The same procedure as already described was followed before each of the follow-up sessions.

2.6 | Outcome measures

Characteristic pain intensity (CPI), measured at the beginning and end of the active study period by means of the GCPS (Version 2.0 derived from DC/TMD), was assessed as the primary outcome. CPI was calculated from NRS values for mean, worst and current pain ((mean pain + worst pain + current pain) ÷ 3 × 10) by a person unaware of the study group allocation. To gauge the course of pain during the active intervention time, a version of the CPI scale that had been modified to consider the previous week only was used before each acupuncture session.

Secondary outcomes comprised the maximum corrected active mouth-opening without pain; patients' expectations regarding acupuncture treatment and pain development (assessed using a customised, six-point Likert scale consisting of three questions as seen in Table 1); depressivity as measured by the German version of the Patient Health Questionnaire (PHQ-9); and oral health-related quality of life (OHRQoL) as measured by the German version of the Oral Health Impact Profile (OHIP-49).

2.7 | Statistics

Because no data were available regarding the effect of acupuncture on CPI reduction of selected non-dysfunctional patients with TMD pain, an a priori sample size calculation was not possible.

All outcome measures were reported descriptively as means and standard deviations. All analysed data were tested for normal

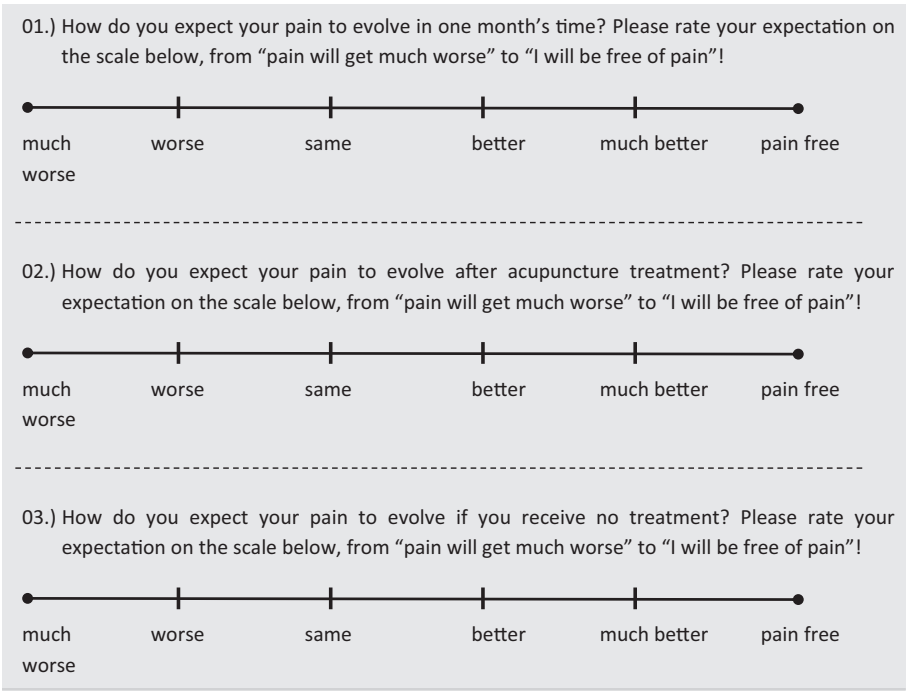

TABLE 1 Custom-made Likert scale questionnaire used to assess patient expectations How do you expect your pain to evolve in one month's time? Please rate your expectation on the scale below, from "pain will get much worse" to "I will be free of pain"!

distribution by use of the Kolmogorov-Smirnov test. Characteristic pain intensity for both groups, as rated using NRS scales, was compared between the five time points (T0-T4) by means of one-way, non-parametric, repeated measures ANOVA. All secondary measures were compared between T0 and T4 by means of paired *t* tests or one-way, non-parametric, repeated measures ANOVA, as indicated.

Characteristic pain intensity, active maximum mouth-opening and the values of the questionnaires (expectations, PHQ-9, OHIP-49) were compared for both groups by use of *t* tests or non-parametric ANOVA for independent samples, as indicated. The significance level was set at $P \leq .05$. *P*-values were adjusted for multiple testing by use of the Bonferroni post hoc test. Statistical analysis was performed with the aid of SigmaPlot 13.0 software (Systat Software). Automatic linear modelling analysis was performed using SPSS 25.0 (IBM Corp.).

3 | RESULTS

Of the 49 patients initially recruited, 22 were randomly allocated to group A (specific points) and 27 to group B (non-specific points). Eight of the patients (four from group A and four from group B) did not complete the study. One patient from group A, who was diagnosed with Takayasu arteritis, suspended her participation shortly after the first examination. Another patient from group A realised he had needle phobia, in contrast to his original statement, and a further patient from the same group decided to stop after the first follow-up for personal reasons. Another patient from group A was pain-free after the first acupuncture session and decided not to continue. Four patients from group B did not adhere to the treatment protocol, two for personal and two for occupational reasons. Thus, the remaining 41 patients (18 from group A and 23 from group B) completed the study protocol successfully and were considered for statistical analysis. The mean age of the subjects was 41.56 ± 17.1 years (range: 22-69 years) for group A and 39.09 ± 16.52 years (range: 20-76 years) for group B. The age of the two groups did not differ significantly at T0 (Kruskal-Wallis one-way analysis of variance on ranks, $P = .528$). Both groups consisted almost exclusively of female patients, except for one male patient in group A and two male patients in group B. The distribution of familiar pain sites as defined by the DC/TMD at baseline (T0) and at the final examination (T5) is presented in Table 2. The mean treatment duration was 24 ± 4.43 days for group A and 23.76 ± 5.7 days for group B. No side effects were reported by any of the participants throughout the entire study.

The average number of days with pain during the active study period, as reported by the patients at T5, was 17.22 ± 11.47 (range 2-30) for group A and 18.43 ± 11.0 (range 1-30) for group B. This did not differ significantly between the two groups (Mann-Whitney rank sum test, $P = .573$). The time course of CPI for each study group between T0 and T5 is shown in Figure 3. CPI values for the two study groups did not differ significantly at either the beginning (T0) or end (T5) of the study (Mann-Whitney rank sum test, $P = .429$ and $P = .722$, respectively). Between T0 and T5, CPI reduced by 29.66% for group A and by 30.38% for group B. These reductions were statistically significant for both groups (Wilcoxon signed rank test, $P < .001$ (A) and $P = .002$ (B)). The post hoc calculation of power for the given sample size revealed an observed power of $\beta = 0.7$ (two-tailed $\alpha = 0.05$).

The course of CPI during the intervention time (four weeks) can be seen in Figure 4. A CPI reduction was observed for both groups, although the pattern in the groups was different. For group A, a significant CPI

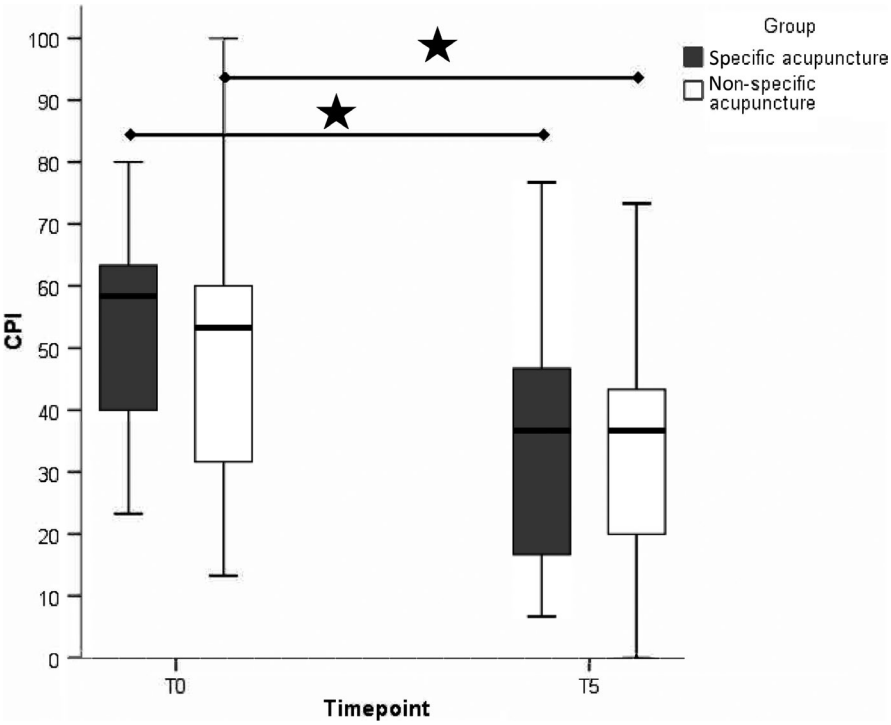

FIGURE 3 Characteristic pain intensity (CPI) for both study groups at the beginning (T0) and end (T5) of the study. The change for both groups was statistically significant (Wilcoxon signed rank test, $P < .05$), as denoted by the stars.

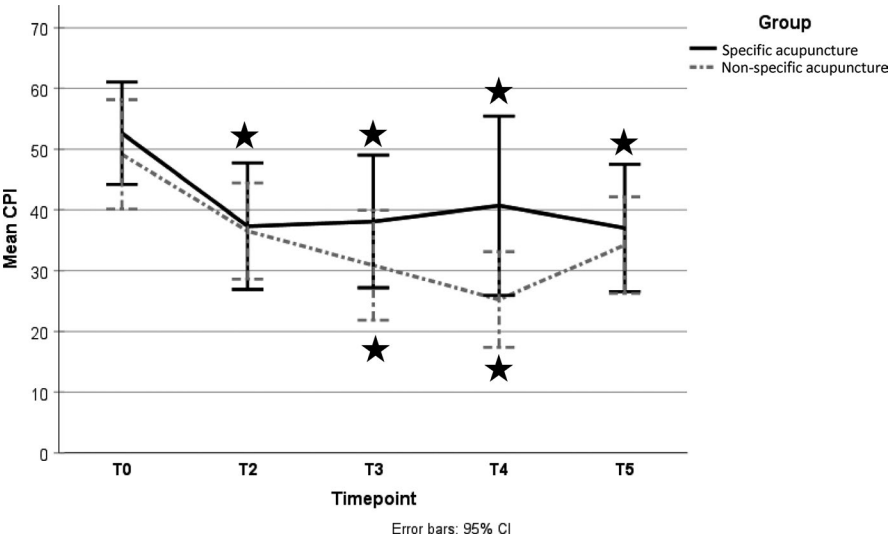

FIGURE 4 Course of characteristic pain intensity (CPI) for both study groups at all study time points (T0 through T5). The change for group A (acupuncture on specific points) was already statistically significant by T2, as denoted by the star, and remained significant until T5 (Friedman repeated measures analysis of variance on ranks, $p<0.05$). CPI reduction for group B (acupuncture on non-specific points) reached statistical significance at T3 and T4, as denoted by the stars, but showed a trend towards regression at T5 (Friedman repeated measures analysis of variance on ranks, $P < .05$).

TABLE 2 Distribution of familiar pain sites according to the DC/TMD examination. T0 = beginning of study, T5 = end of study

Familiar pain site	Percentage (%) at T0	Percentage (%) at T5
No pain	0.00	9.80
Mast. muscle	21.95	22.00
TMJ	4.88	2.40
Mast. muscle + TMJ	73.17	65.90
Total	100 (n = 41)	100 (n = 41)

reduction of 28.92% had already occurred by T2 (Friedman repeated measures analysis of variance on ranks, $P = .032$), and this remained significant throughout the observation period until T5 (−29.63%) (multiple comparisons versus T0 using Dunnett's method, $P < .05$). For group B, the reduction was also significant overall (Friedman repeated measures analysis of variance on ranks, $P = .002$) and differed significantly from T0 (multiple comparisons using Dunnett's method, $P < .05$) at T3 (−37.15%), T4 (−48.61%), and T5 (−30.38%).

The maximum corrected active mouth-opening without pain (MAO) differed significantly between the two treatment groups at T0 (t test for independent samples, $t(39) = 2.276$; $P = .028$). An increase in MAO was observed at T5 for both groups, but was significant for group B only (paired t test, $t(22) = -2.597$; $P = .016$), as seen in Table 3 and Figure 5.

The vast majority (87.8%) of participants had predominantly positive expectations regarding their pain course within the coming 30 days, but only three (all in group B) expected to be free of pain

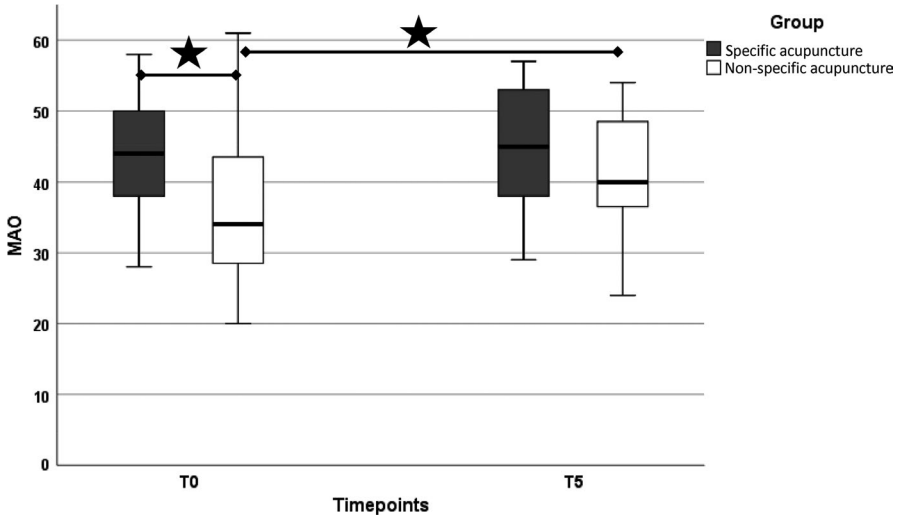

FIGURE 5 Corrected active maximum mouth-opening without pain (MAO) for both study groups at the beginning (T0) and end (T5) of the study. The statistically significant differences (*t* test for independent and paired samples, $P < .05$) are denoted by the stars.

in this time. All patients had positive expectations of acupuncture therapy (six expected to be free of pain, of whom five were from group B), and the opposite was observed for patient expectations of no treatment (only four had positive expectations, of whom three were from group B). The expectations of no treatment differed significantly between the groups (Kruskal-Wallis one-way analysis of variance on ranks, $P < .001$). The inter-group comparison showed that the difference in median values at T0 between the two study groups was significantly greater (group B had more positive expectations than group A) than expected by chance for the item of general pain course (Mann-Whitney rank sum test, $P = .009$). At T5, the two groups did not differ significantly with regard to the extent to which their expectations had been fulfilled by the treatment (Mann-Whitney rank sum test, $P = .717$).

Oral health-related quality of life (OHRQoL), as indicated by the total score of the OHIP, did not differ significantly between the two treatment groups at T0 (Mann-Whitney rank sum test, $P = .703$) or at T5 (Mann-Whitney rank sum test, $P = .906$). At T5, the overall OHIP score had improved significantly for both groups (Wilcoxon signed rank test: group A, $P = .018$; group B, $P < .001$) compared with at T0. A comparison of the individual OHIP domains by means of the Wilcoxon signed rank test also revealed a significant reduction in scores for physical pain (group A, $P = .014$; group B, $P = .003$), psychological discomfort (group A, $P = .032$; group B, $P = .002$), physical disability (group A, $P = .048$; group B, $P = .050$), psychological disability (group A, $P = .033$; group B $P < .001$), social disability (group B $P < .001$) and handicap (group A, $P = .031$; group B, $P = .008$). In contrast, a significant score reduction was not seen for the domains of functional limitation (group A, $P = .208$; group B, $P = .063$) and social disability (group A, $P = .158$), nor for the four additional items included in the German version of the OHIP (group A, $P = .163$; group B, $P = .082$).

The level of distress, as measured using the German version of the PHQ-9, did not differ significantly between the two treatment groups at T0 (*t* test for independent samples, $t(39) = 1.105$; $P = .276$) or at T5 (*t* test for independent samples, $t(39) = -0.254$; $P = .801$). Comparison of T0 and T5 showed a statistically significant reduction of the PHQ-9 score for group A (paired t test, $t(17) = 2.554$; $P = .0205$), but no significant change for group B (paired *t* test, $t(22) = 0.999$; $P = .329$).

TABLE 3 Corrected active maximum mouth-opening without pain (in mm)

	T0	T5	T0 vs T5 (paired *t* test)
Protocol A (n = 18)			
Mean (SD)	43.33 (9.36)	44.67 (9.21)	$P = .336$
Range	28-58	29-57	
Protocol B (n = 23)			
Mean (SD)	35.96 (10.97)	41.04 (8.74)	$P = .016$*
Range	20-61	24-54	
Protocol A compared with B (*t* test)	$P = .028$*	$P = .206$	
Total (n = 41)			
Mean (SD)	39.20 (10.82)	42.63 (9.02)	

Protocol A = acupuncture on specific points; Protocol B = acupuncture on non-specific points; Asterisks denote statistically significant differences.

To identify the most important item among the large number of predictors of pain reduction at T5, as measured for both groups using the CPI scale, we used an "all possible regressions" algorithm (available as automatic linear modelling in the statistical package SPSS version 25.0). The target variable was the percentage change in CPI between T0 and T5, and the following predictors were inserted in the model: gender; age; group allocation; number of days with TMD pain; corrected maximum active opening without pain; expectations regarding pain course; expectations regarding the treatment effect of acupuncture and expectations regarding the effect of no treatment; degree of distress; location of familiar pain sites; patient's account of sleep and awake bruxism; patient's account of headaches; OHRQoL; and the extent to which expectations were fulfilled. The forward stepwise standard model created yielded an accuracy of 37.2%, which is quite low. The most important predictors appeared to be the extent to which expectations were fulfilled, age and the number of days with TMD pain (Table 4).

4 | DISCUSSION

The results of this single-centre two-arm parallel-group double-blinded randomised controlled trial could not confirm the initial hypothesis that specific acupuncture points would be superior to non-specific ones for the treatment of non-chronic painful TMDs. Both protocols reduced non-dysfunctional, TMD-associated orofacial pain significantly, but the reduction was at the edge of clinical significance (approximately 30%) as defined by the IMMPACT statement.[27] This reduction could, however, still be observed after five to six weeks. Interestingly, the course of pain reduction followed a different pattern in each group. In contrast to the non-specific points group, group A had already experienced a significant reduction in pain by T2, which remained significant until T5. The non-specific points group reached statistical significance for pain reduction at T3 and T4, although this effect had decreased by T5.

The WHO estimates that one-third of the world's population has no regular access to modern medicine, especially in many parts of Africa, Asia and Latin America. Fortunately, complementary and alternative treatments such as herbal and traditional medicine and acupuncture are available and accessible[28] (accessed on April 17 2019). Acupuncture seems to significantly reduce TMD pain, but is not efficient when used as a single first-line treatment. One advantage of this technique is its absence of side effects, and a possible combination of (even non-specific) acupuncture with other standard treatment procedures for painful TMDs, such as oral splints, home exercise might yield better results than conventional therapies alone. It might therefore benefit patients to integrate acupuncture with other types of conventional treatments.

One advantage of this study was its selection of patients with non-dysfunctional TMD pain, the objective of which was to make the sample more representative of the majority of patients treated in first-line clinical settings. In TCM, a given disease does not correspond to a specific selection of acupuncture points. The TCM treatment protocol instead focuses on the TCM diagnosis, which includes the interactions between disorders, pain or dysfunctionality of an organ system; these are associated with so-called meridians and the constitution of the individual. As a result, painful TMDs might be treated using different points for each individual. This explains why studies recommend different points for the treatment of painful TMDs, for example, local painful point and distal point LI-4[29]; ST-7[30]; and ST-6, SI-18 (local), SI-3, and LI-4 (distal).[31] In our study, we selected our treatment points according to a pilot study of the TCM diagnosis of non-chronic (GCPS < 3) painful TMDs. The common denominator of the TMD-associated meridians was selected for the standardisation reasons explained above, resulting in five local (BL-2, BL-3, SI-19, ST-7 and TE-21) and two distal (BL-34 and SI-3) points, in addition to the ear acupuncture point. Points ST-7 and SI-3 were in agreement with other studies.[18,31] The treatment duration in our study was also reasonable. Unfortunately, it was not feasible to extend the acupuncture intervention to more than four sessions, and we have no further data regarding the stability of the treatment effect after the end of the intervention. This is another limitation of our study. A recent meta-analysis found that a full course of acupuncture treatment consisted of 1-6 sessions over three weeks, with each session lasting 15-30 minutes.[18]

TABLE 4 Factors identified as significant in the regression analysis with automatic linear modelling

Source	Sum of Squares	*df*	Mean Square	*F*	Significance	Importance
Corrected Model	20 237.026	3	6745.675	8.907	**0.000**	
Fulfilment of expectations[a]	9349.288	1	9349.288	12.344	**0.001**	0.533
Age[a]	4626.888	1	4626.888	6.109	**0.018**	0.264
Days with pain[a]	3561.994	1	3561.994	4.703	**0.037**	0.203
Residual	28 022.517	37	757.365			
Corrected Total	48 259.543	40				

[a]Transformed values.

Significance values are marked in bold.

4.1 | Possible mechanism of action of acupuncture

According to the viewpoint of Western medicine, acupuncture's mechanism of action for TMD pain treatment might result from changes in the level of neurotransmitters such as dopamine, opioid derivates, met-enkephalin and substance P along the nociceptive pathway. Other explanations for acupuncture's mechanism of action (eg that it results from the interaction between two systems, the fascia connective tissue system and primo vascular system, via peripheral and central inflammatory factors) have recently been reviewed.[32-34] Previous studies showed that acupuncture can decrease peripheral, pro-inflammatory cytokines such as TNF-α, IL-1β and IL-6; corticotrophin-releasing factor; COX-1 and 2; and prostaglandin E2 (PGE2).[34] With regard to pain modulation, other factors might also have an effect, including the possible effects of conditioned pain modulation/diffuse noxious inhibitory control (DNIC) [35]; tissue injury reaction as a response to the interruption of dermal continuity; and effects arising from the stimulation of dermal nociceptors. However, the effect of these factors in the context of acupuncture is not yet clear.

4.2 | Non-specific acupuncture points, expectations and the placebo effect of acupuncture

The non-specific acupuncture points chosen for this study have no connection to the meridians of TCM. Nonetheless, although needles were inserted at "non-specific" acupuncture points, this cannot be considered an inert intervention from the viewpoint of Western medicine. It could be argued that it was impossible to show differences between specific and non-specific acupuncture groups because non-specific points do not actually exist in the neurobiological model.[33] Studies have reported a significantly greater treatment effect for acupuncture when compared with sham acupuncture using non-penetrating needles, whereas the difference appeared smaller in trials that used needle penetration in the control group. These studies also found significant differences between trials using penetrating needle sham and those using non-penetrating or non-needle sham.[12,23] Some researchers claim that a consensus will never be reached on whether sham or placebo acupuncture is the more appropriate control for clinical trials of acupuncture.[36]

Other acupuncture protocols, such as placebo acupuncture using the needle developed by Streitberger and Kleinhenz,[37] give the impression of skin penetration without actually piercing the skin. Such options act like a stage dagger, with the needle disappearing into the needle shaft, and have been observed to be as effective as placebo acupuncture.[38] In our study, we used penetrating needle acupuncture in non-specific points outside the main meridians. This was an attempt to ensure that patients were unaware whether they were receiving a specific or non-specific approach, which would have otherwise been at risk in our clinical setting (ie patients could check the presence of needles). According to current understanding, the placebo effect is a genuine psychobiological event attributable to the overall therapeutic context, that is to individual patient and clinician factors, and the interaction between the patient, clinician and treatment environment.[39] We tried to minimise the placebo effect of the environment by decreasing the interaction between the "therapist" and participants, and by keeping the "ritual" of acupuncture as simple as possible [40] and ensuring that a common clinic room with only one hospital bed was used. Carlsson and Sjolund[41] showed that the effect of acupuncture on chronic low back pain might be superior to that of a placebo in the long term, that is in the follow-up after one month. Therefore, the remission of pain reduction four weeks after the first non-specific acupuncture appointment observed in our study might be in line with these findings.

The neurobiological mechanisms of the analgesic effects of a placebo include the activation of endogenous opioids, dopamine release and the alteration of the central processing of pain.[39,42,43] Although it is suggested that placebos can relieve pain arising from physiological causes and have an average significant effectiveness of 35.2 ± 2.2%,[44] it is difficult to assess the extent of the placebo analgesic effect because experimental conditions can differ between studies. Recent studies showed that cognitive factors such as context, beliefs, culture, previous experiences, prejudices, expectations substantially influence the placebo effect. It is usually hard to perform a clinical study that takes these cognitive factors into account.[45]

The selection of particular acupuncture points might also be more important than previously thought. In group A, the specific acupuncture points were located above muscle tissue; hence, the needle that penetrated the subcutaneous tissue to a depth of 1 cm predominantly landed in muscle tissue. The non-specific points in group B, in contrast, were located above the fat tissue on the lateral waistline, meaning that the same penetration depth through the subcutaneous tissue resulted in penetration of a different tissue type. Possible differences in nociception between the different tissues might account for the effects observed.

The expectation of benefits also substantially affects the efficacy of placebo interventions.[38,39,42,43,46-49] Expectations can modify pain perception in the brain, and studies of dental patients showed that patients' beliefs about acupuncture bore a considerably more powerful relationship to pain than any specific action of the acupuncture itself.[46] In view of the fact that all the patients in our study received the same information in a standardised manner at T0, the considerably higher expectations of group B (non-specific points) might account for their significant pain reduction at T3 and T4. In any case, the high expectations experienced by most participants might be associated with visiting a specialised clinic, that is the acupuncture was accepted as a legitimate and effective medical procedure. In the absence of data on the role of expectations in oro-facial pain treatment, we suggest that expectations should be addressed by means of simple questions and taken into account when assessing the effectiveness of treatment types. This suggestion is based on our results and is in agreement with the literature.[48] The higher the expectations, the greater the placebo

effect, and potentially the greater the conditioning effects associated with future interventions.[39] If patient expectations play a crucial role in determining the outcome of an acupuncture trial, then researchers might also be strongly biased in favour of or against the efficacy of acupuncture, which might likewise affect the overall outcome of a trial. To take the latter into account, this study was designed and carried out by two dentists who had no professional experience of acupuncture and a fairly neutral opinion of TCM. Nevertheless, all patients in both groups had positive expectations of acupuncture. In contrast, group B had significantly higher expectations of no treatment than group A did. Even if non-specific acupuncture does not correspond to "no treatment," this could nonetheless have affected the results in group B. This is a limitation of our study.

4.3 | Counselling

Previous studies with a similar patient sample[50] showed that counselling has an early effect, resulting in a CPI drop of approximately 23% within two weeks. In our study, all patients received the same information in a standardised manner. The course of CPI (Figure 4) shows a reduction in CPI at T2 (1-2 weeks after counselling and one week after the first acupuncture session) was 28.92% for group A and 25.67% for group B. The extent of this reduction could represent the combined effect of counselling and (specific or non-specific) acupuncture treatment. The small surplus observed in group A might represent the small specific effect of the acupuncture treatment in the first week.

4.4 | Quality of life and distress

The improvement in OHRQoL for both groups might be related to the overall significant reduction in pain. Further analysis of the main domains of the OHIP also showed a significant improvement in OHRQoL for the domains of psychological discomfort, physical disability, psychological disability, handicap and (group B only) social disability. Studies have shown that acupuncture improves the OHRQoL of women with breast cancer[51] and of patients with burning mouth syndrome.[52] For patients with chronic sinusitis, however, the effect of acupuncture at non-specific points on short-term OHRQoL outcomes was not observed to be superior to that of placebo or sham acupuncture.[53] The reduction of distress in group A might be attributed to acupuncture and explained by the assumed effects of acupuncture on glutamate in neuropsychiatric disorders such as depression, anxiety and schizophrenia, and on glutamatergic neurotransmission in Alzheimer's disease.[54]

4.5 | Further limitations

One limitation of our study is the absence of a waiting list group. This would have enabled us to control for natural history and regression to the mean. The creation of such a group for the length of the intervention and observation period (at least 6 weeks) is not compatible with ethical standards; hence, this was not allowed by the ethics committee. Although waiting list groups were usually subject to long waiting times, they were nonetheless used as controls in acupuncture trials until the end of 1990s, which coincides with the shift towards more rigorous ethical standards in clinical trials. Another limitation of our study is its quite short observation time. Nevertheless, because the study participants had acute or acute-persistent pain (without signs of dysfunctional pain chronification), it was realistic to expect treatment effects in a period of 6-8 weeks. This shortcoming should be addressed in future studies.

5 | CONCLUSION

Within the limitations of this study, which mostly relate to the small number of participants and lack of baseline equivalency of expectations, we observed a significant but non-specific reduction in pain among patients with non-chronic painful TMD after four weeks of acupuncture treatment. This reduction was on the margin of clinical significance. Acupuncture (specific or not) should therefore be considered as a first-line treatment option, preferably in combination with other treatments. Further studies are warranted to study the long-term effects of acupuncture treatment on TMDs.

ACKNOWLEDGMENTS

The authors thank Hazel Davies MSc (UCL) for critically reading the manuscript.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

S. Şen and NN Giannakopoulos: involved in conceptualisation, project administration, methodology, investigation, supervision of investigators, data curation, original draft preparation, reviewing and editing; G. Orhan: involved in investigation and data curation; S. Sertel: involved in conceptualisation, reviewing and editing; H. J. Schindler: involved in conceptualisation, methodology, original draft preparation, reviewing and editing; C. J. Lux and M. Schmitter: involved in reviewing and editing. All authors critically revised the manuscript for important intellectual content, gave approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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How to cite this article: Şen S, Orhan G, Sertel S, et al. Comparison of acupuncture on specific and non-specific points for the treatment of painful temporomandibular disorders: A randomised controlled trial. *J Oral Rehabil*. 2020;47:783–795. https://doi.org/10.1111/joor.12952