Acupuncture

Chapter 2

Acupuncture in Primary Headache Disorders

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1. Introduction

Acupuncture is part of traditional Chinese medicine, which has been used for treatment in headache disorders as well as for other health conditions. It is an ancient practice which has been used for thousands of years and the original theory is based on altering 'Qi' which is believed to run through certain 'meridians' [1]. In recent years, studies have investigated the neurobiological basis of acupuncture and a number of theories have been proposed for its mechanism in various health disorders [2].

A number of trials asked whether acupuncture is clinically effective but the nature of the intervention makes it difficult to assess through modern medical methods where randomized double blind controlled trials are considered as the gold standard. It is hard to achieve a true control arm as we still do not fully understand the mechanism of action for acupuncture. Studies have tried to use 'sham' acupuncture whereby either non-traditional acupuncture points were selected or non-penetrating needles were used. It has however been proposed that the local effects of a needle insertion in non-traditional acupuncture points may cause physiological change [2]. Others compared acupuncture with no acupuncture but this risks a significant placebo effect. Another potential challenge is that different acupuncture points have been used for the same clinical condition, which may make interpretation of the results difficult.

To assess this growing evidence, Cochrane reviews have recently been published on acupuncture in migraine [3] and tension type headaches [4]. Recently, the National Institute of Clinical Excellence (NICE) has issued some guidance for the use of acupuncture in primary headache disorders in the UK [5]:

For prophylaxis of migraine:

● 'If both topiramate and propranolol are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over 5-8 weeks according to the person's preference, comorbidities and risk of adverse events.'

For prophylaxis of tension type headache:

● 'Consider a course of up to 10 sessions of acupuncture over 5-8 weeks for the prophylactic treatment of chronic tension-type headache'

This chapter aims to provide an up to date review on the evidence surrounding the clinical effectiveness of acupuncture in primary headache disorders followed by a discussion on its safety, tolerability and cost economics.

2. Migraine

Migraineurs are described to have chronic migraine if they have 'headache occurring on 15 or more days/month for more than 3 months, which, on at least 8 days/month, has the features of migraine headache' according to the International Classification of Headache Disorders 3rd Edition [6]. A frequency less than this is episodic migraine.

2.1 Episodic migraine

A recent Cochrane review has evaluated the use of acupuncture in episodic migraine [3]. There are important differences in the methodology to the previous Cochrane review [7]. Participants were now excluded if they had chronic migraine or migraine for less than 12 months duration on average. The review only included trials in which the participants were randomized and followed up for at least 8 weeks. It now includes other trials which compared acupuncture to prophylactic medications. The latest review included 22 trials with a total of 4985 participants [3].

The Cochrane review divided the analysis into acupuncture versus no acupuncture, acupuncture versus sham acupuncture and acupuncture versus standard prophylactic medications.

2.1.1 Acupuncture versus no acupuncture

Some of the studies comparing acupuncture to control are shown in **Table 1**. In the Cochrane review, a combined analysis of 4 studies [8-11] showed a reduction in headache frequency for acupuncture versus control at 3 months (standardized mean difference -0.56 (-0.65 to -0.48)) [3]. In the same 4 studies, the 50% responder rate was 41% versus 17%, for acupuncture versus control respectively, giving a risk ratio of 2.40 (2.08-2.16) [3]. The number

needed to treat was calculated to be 4. One study [9] was followed up for 12 months and also showed a reduction in headache frequency in the acupuncture group compared to controls (standardized mean difference -0.36 (-0.59 to -0.12)) [3]. The 50% responder rate risk ratio was 2.16 (1.35-3.45) giving a number needed to treat of 7 [3].

One study published after the Cochrane review in 2017 also showed that acupuncture was superior to control in both reducing migraine days as well as intensity of migraine [12]. Jena et al included a large number (n=11,874) of non-randomized subjects who received acupuncture [11]. As it was not randomized, these subjects were not included in the Cochrane analysis but the authors claim that the outcomes were similar to the randomized subjects [11]. Facco et al used the MIDAS (Migraine Disability Assessment) score as outcome and found that acupuncture significantly reduced MIDAS scores, as well as the number of abortive rizatriptan tablets used, compared to control at both 3 and 6 months [13].

Table 1: A table to show some of the studies comparing acupuncture versus no acupuncture in migraine.

Study	n	Methodology	Results
Linde M et al 2000 [8]	Acu 11 Control 12	RCT 7-10 acupuncture sessions over 4-6 weeks; follow up 12 weeks Outcomes: Migraine days Medication use	• No significant difference in outcome between acupuncture and control groups. • High dropout rate, 45% in the acupuncture group and 37% in the control group
Vickers et al 2004 [9]	Acu 205 Control 196	RCT 12 acupuncture sessions over 3 months; follow up 9 months Outcomes: Headache score Headache days Use of medications	• Headache score lower in the acupuncture group (18.0±14.8) compared to controls (23.7±16.8) at the end of treatment at 3 months, *p=0.001* • Headache score lower in the acupuncture group (16.2±13.7) compared to controls (22.3±17.0) at 12 months, *p=0.0002* • Number of headache days per 28 days lower in acupuncture (12.1±7.2) compared to controls (14.3±7.3) at the end of treatment at 3 months, *p=0.002* • Number of headache days per 28 days lower in acupuncture (11.4±7.5) compared to controls (13.6±7.5) at 12 months, *p=0.003* • No difference in proportion who used prophylactic medications at 3 months but smaller proportion used in acupuncture (14%) compared to 26% at 6 months, *p=0.005*
Linde K et al 2005 [10]	Acu 145 Sham 81 Control 76	• RCT • 12 sessions over 8 weeks; follow up 16 weeks • Sham used superficial needling at non-acupuncture points • Outcomes: • Headache days	• Acupuncture no significant difference to sham acupuncture in headache days at 12 weeks *(p=0.96)* • Difference of 1.4 (0.8-2.1) headache days when comparing acupuncture to control at 12 weeks *(p<0.001)*

Facco et al 2008 [13]	TA 32 R 34 RMA 30 SMA 31 Total 127	• RCT • 4 groups (TA, R, RMA, SMA) • 20 sessions of acupuncture over 11 weeks; follow up 3 months • RMA used non penetrating needles at same points as TA • SMA Western approach for diagnosis and uses non-penetrating needles in standard acupoints • Outcome: MIDAS score	• TA and RMA shows significant reduction in MIDAS index compared to R at 3 months *(p<0.0001)* • Only TA significant reduction in MIDAS index over R at 6 months *(p<0.0001)* • Only TA shows significant reduction in number of rizatriptan tablets over R at 3 and 6 months *(p<0.0001)*
Jena et al 2008 [11]	Acu 1613 Control 1569 (Migraine or tension type headaches)	• RCT • Subjects had migraine or tension type headache • Up to 15 sessions acupuncture over 3 months; no follow up • Controlreceived acupuncture after 3 months so becomes non-randomized (not statistically compared in Cochrane review) • Also 11,874 non-randomized patients received acupuncture (not statistically compared in Cochrane review) • Outcomes: Headache days reduction, Pain intensity, Quality of life	• Mean headache days decreased from 8.4±7.2 to 4.7±5.6 in the acupuncture group versus 8.1±6.8 to 7.5±6.3 in the control group at 3 months *(p<0.001)* • Pain intensity and quality of life significantly improved in acupuncture versus control group at 3 months *(p<0.001)* • Outcome changes in non randomized patients similar to randomized patients
Zhao et al 2017 [12]	Acu 83 Sham 80 Control 82	• Randomized • Electrostimulation • 20 sessions acupuncture over 4 weeks; follow up 20 weeks • Sham used non-acupuncture points • Outcomes: Change in frequency of migraine Migraine days Average headache severity Use of medication	• Greater mean reduction in frequency of migraine attacks from baseline in acupuncture (3.2 ± 2.1) versus sham (2.1 ± 2.5) at 16 weeks, *p=0.002* • Greater mean reduction in frequency of migraine attacks from baseline in acupuncture (3.2 ± 2.1) versus control (1.4 ± 2.5) at 16 weeks, *p<0.001* • Sham was not statistically different to control in reducing the frequency of migraine attacks at 16 weeks • Greater mean reduction in frequency of migraine days in acupuncture versus sham and acupuncture versus control • Lower VAS score in acupuncture versus sham and in acupuncture versus control • Also lower VAS score in sham versus control

TA: True acupuncture; RMA: Ritualized mock acupuncture; SMA: Standard mock acupuncture; R: Relief therapy only (without prophylactic therapy); MIDAS: Migraine disability assessment; TCM: Traditional Chinese medicine; Acu: Acupuncture; RCT: Randomized controlled trial; QALY: Quality adjusted life years

2.1.2 Acupuncture versus sham acupuncture

A number of studies looked at the comparison between 'true acupuncture' and 'sham acupuncture'. The manner in which the investigators create sham acupuncture varies between studies, with a combination of using non-acupuncture/non-indicated points and superficial/non-penetrating needles (Table 2).

Some of these studies show no significant difference in headache days between true acupuncture and sham [10,14-16]. Other studies show an improvement with true acupuncture in headache days compared to sham [12,17-20]. In a Cochrane pooled analysis in 2016, there was a statistically significant reduction in headache frequency comparing true acupuncture to sham acupuncture after treatment (standardized mean difference -0.18 (-0.28 to -0.08)) and at a median 6 months follow up (standardized mean difference -0.56 (-0.65 to -0.48) although the differences were small [3]. The 50% responder rate was 50% in acupuncture versus 41% in sham, after treatment and 53% in acupuncture versus 42% in sham, at a median 6 months follow up. This yields 50% risk ratio of 1.23 (1.11 - 1.36) and a number needed to treat of 11 after treatment and a risk ratio of 1.25 (1.13 - 1.39) and a number needed to treat of 10 at follow up [3].

One group looked at the effects of 3 different true acupuncture points compared to sham acupuncture [20]. They found no difference between the 3 true acupuncture groups in terms of both migraine frequency and intensity, but all were statistically superior to sham. The Zhao et al 2017 study published after the Cochrane review showed that true acupuncture reduced the frequency of headache days more than sham and control at 16 weeks, whereas sham was no different to control at 16 weeks [12]. Facco et al showed both true acupuncture and sham acupuncture reduced MIDAS (Migraine Disability Assessment) scores significantly when compared to control at 3 months, but only true acupuncture was superior at 6 months [13]. True acupuncture (but not sham acupuncture) resulted in fewer rizatriptan tablets used [13]. Some studies also looked at the effect of acupuncture on migraine intensity **(Table 2)**, with some reporting no difference [14] but others reporting superiority with acupuncture over sham [12,14,18-20].

Table 2: A table to show some of the studies comparing acupuncture versus sham acupuncture in migraine.

Study	n	Methodology	Results
Linde K et al 2005 [10]		See Table 1	See Table 1
Linde M et al 2005 [14]	Acu 15 Sham 13	• Randomized • Women with menstrual migraine • 9 acupuncture sessions in 3 months; follow up 6 months • Sham used non-penetrating needles at same point • Outcomes: Headache frequency, • Headache intensity, Drug use	No difference between acupuncture and sham groups at 3 and 6 months follow up for attack frequency, headache intensity or drug use
Alecrim et al 2006 [15]	Acu 16 Sham 15	• Randomized • 16 acupuncture sessions in 12 weeks; follow up 24 weeks • Sham used superficial needling at non-indicated points • Outcomes: • Proportion with reduction >40% and >50% in headache days • Migraine days Average duration of migraine attack Rate of rescue medication used	No statically significant differences between real or sham acupuncture in the outcomes
Diener et al 2006 [16]	Acu 313 Sham 339 Drug 308	• Randomized multicenter • 10 acupuncture sessions in 6 weeks; follow up 20 weeks • Sham used superficial needling at non-acupuncture points • Continuous prophylactic drug (beta blockers/ flunarizine/valproic acid) • Outcome: Migraine days at 23-26 weeks	• All 3 interventions significantly reduced migraine days at 23-26 weeks compared to baseline, $p<0.001$ • No difference in the reduction in migraine days between the 3 groups
Alecrim et al 2008 [17]	Acu 19 Sham 18	• Randomized • 16 acupuncture sessions in 12 weeks; follow up 24 weeks • Sham used superficial needling at non-indicated points • Outcomes: Percentage with >50% reduction in headache days Number of migraine days Percentage with >40% reduction in headache days	• Statistically significant improvement with acupuncture versus sham in the primary endpoint ($p=0.021$) • Statistically significant differences with acupuncture versus sham in 2 secondary endpoints • Statistical significance present in the first and second month but disappears by the third month
Facco et al 2008 [13]		See Table 1	See Table 1

Li et al 2012 [20]	Acu (SS) 121 Acu (SN) 119 Acu (Y) 118 Sham 118	• Randomized • Electrostimulation • 20 acupuncture sessions in 4 weeks; follow up 16 weeks • 3 acupuncture groups (Shaoyang specific, Shaoyang non specific, Yangming specific) • Sham used non-acupuncture points • Outcomes: Migraine days weeks 5-8 weeks after randomization • Frequency of migraine attack Migraine intensity (VAS)	• All 3 acupuncture groups, individually not statistically different in headache days to sham at 5-8 weeks • All 3 acupuncture groups, individually compared to sham acupuncture showed statistically reduced headache days, by 13-16 weeks • Comparing between the 3 acupuncture, no difference in headache days at any follow up between the 3 acupuncture groups • All 3 acupuncture groups, individually compared to sham showed reduction in migraine frequency at both 5-8 weeks and 13-16 weeks • No difference in migraine frequency at any follow up between the 3 acupuncture groups • All 3 acupuncture groups, individually compared to sham showed reduction in intensity (VAS) at 13-16 weeks
Zhao et al 2014 [19]	Acu 40 Sham 40	• Randomized • 32 acupuncture sessions in 8 weeks; no follow up • Sham used non-indicated points • Outcomes:Severity (VAS)duration and frequency of headaches in diary HIT-6 score	• Significantly more reduction in mean headache intensity by VAS score compared to baseline in acupuncture (2.096 ± 0.25) versus sham (1.110 ± 0.25) at week 8 • No significant differences between the two groups for frequency of migraine, number of days with migraine and HIT-6 score at week 8
Wang et al 2015 [18]	Acu 26 Sham 24	• Randomized • 16 acupuncture sessions over 20 weeks; follow up 3 months and 1 year • Sham used non-penetrating blunted stick/ superficial needle insertion in sham locations • Outcomes: Migraine days over 4 weeks Duration and intensity of migraine (VAS) Number of 50% responder Use of relief medications Intensity of migraine Quality of life Pressure pain thresholds	• Significantly less migraine compared to baseline for acupuncture (5.2 ± 5.0) compared to sham (10.1 ± 7.1), (*p=0.008)* • Significantly less intense in acupuncture group compared to sham (*p=0.004)* • More 50% responders with acupuncture compared with sham(19 versus 7) • Increased pressure pain thresholds • No other significant differences found • The group differences not maintained at 1 year follow up
Zhao et al 2017 [12]		See Table 1	See Table 1

Acu: Acupuncture; VAS: Visual analogue scale: HIT - 6: (6 item) Headache impact test; SS: Shaoyang specific; SN: Shaoyang nonspecific; Y: Yangming specific

2.1.3 Acupuncture versus prophylactic drug treatment

In the Cochrane review [3], a combined analysis of 3 studies [16,21,22] show that migraine frequency was significantly reduced for acupuncture versus drug prophylaxis at median 3 months follow up (standard mean difference -0.25 (-0.39 to -0.10), p=0.001) . There was no significant difference in migraine frequency at 6 months follow up. The 50% responder rate for acupuncture and prophylactic drugs were 57% and 46% at 3 months, and 59% and 54% at 6 months, respectively. The respective risk ratios for acupuncture versus prophylactic drugs were 1.24 (1.08 to 1.44) after 3 months and 1.11 (0.97 to 1.26) after 6 months [3]. It should be noted that the 3 trials used different prophylactic drugs (**Table 3**).

One study compared acupuncture with 600mg daily of Valproate [23]. They assessed differences in intensity using visual analogue scale (VAS) and found valproate to be superior at 3 months but acupuncture to be superior at 6 months. A recently published meta-analysis assessed acupuncture versus propranolol using indirect treatment comparison [24]. This analysis shows that acupuncture significantly reduced more migraine episodes and resulted in lower migraine frequency over 4 weeks compared to propranolol.

Table 3: A table to show some of the studies comparing acupuncture versus prophylactic medications in migraine.

Study	n	Methodology	Results
Allais et al 2002 [22]	Acu 80 Drug 80	• Randomized • 12 acupuncture sessions in 6 months; no follow up • **Flunarizine** 10mg daily for first 2 months and then for 20 days per month for next 4 months • Outcomes: Number of attacks at 2 and 4 months Migraine Intensity	• Significantly lower number of attacks in acupuncture versus flunarizine at both 2 and 4 months • No difference in number of attacks between acupuncture versus flunarizine at 6 months • Pain intensity was significantly reduced only by acupuncture
Diener et al 2006 [16]		See Table 2	See Table 2
Streng et al 2006 [21]	Acu 59 Drug 55	• Randomized • Up to15 acupuncture sessions in 12 weeks; follow up 12 weeks • **Metoprolol** 100-200mg daily • Outcomes: • Difference in migraine days between baseline and weeks 9-12	• No difference in the reduction of migraine days from baseline between acupuncture (2.5 ± 2.9) and metoprolol (2.2 ± 2.7), *p=0.721* • 50% responder rate of 61% (acupuncture) and 49% (metoprolol) • High dropout rate in metoprolol group 18/55 so results need to be interpreted with caution

Facco et al 2013 [23]	Acu 50 Drug 50	• Randomized • 20 acupuncture sessions in 3 months; follow up 3 months • **Valproate** 600mg/day • Rizatriptan 10mg wafers prn allowed • Outcomes: MIDAS index and VAS Six point pain relief score Rizatriptan intake	• In both acupuncture and valproate, the MIDAS index improved at 3 and 6 months • At 3 months, VAS, better in valproate versus acupuncture • At 6 months, VAS, pain relief score, rizatriptan intake better in acupuncture versus valproate

Acu: Acupuncture; MIDAS: Migraine disability assessment; VAS: Visual analogue scale

2.2 Chronic Migraine

A few studies have investigated the use of acupuncture in chronic migraine but these have been excluded for analysis in the latest Cochrane review [3].

In one Iranian study, subjects with chronic migraine were randomized to receive acupuncture, botulinum toxin injection or valproate prophylaxis [25] (Table 3). The mean number of headache days at 3 months reduced in acupuncture group from 21.4 to 8.0, in valproate group from 19.1 to 13.1 and in botulinum toxin group from 23.6 to 13.1 [25]. As an indirect comparison, in the pooled results of original PREEMPT trials, the mean reduction was 8.4 headache days at 6 months for botulinum toxin group [26]. Comparison between the 3 groups in this Iranian study show a greater reduction in migraine days per month with acupuncture (p=0.0001) [25]. Similarly there was a greater reduction in VAS and number of times requiring medication with the acupuncture group [25]. The 2 studies by Yang show acupuncture is as good or better than topiramate in chronic migraine [27,28]. Another study found that combining acupuncture with Tanacetum (a herbal treatment for migraine) results in better migraine intensity, MIDAS and quality of life scores than either acupuncture or Tanacetum alone [29].

Table 4: A table to show some of the studies on acupuncture in chronic migraine.

Study	n	Methodology	Results
Yang et 2009 [27]	Acu 12 Drug 12	• Randomized • 24 acupuncture sessions in 12 weeks; no follow up • **Topiramate** 25mg/day increasing by 25mg weekly until 100mg/day then maintenance for 8 weeks • Outcomes: Reduction in migraine days Reduction in migraine attacks MIDAS	• Migraine days reduced from 22.2 to 12.8 (40.1%) in the acupuncture group versus 22.7 to 13.8 (37.8%) in the topiramate group • Migraine attacks reduced from 13.3 to 8.0 (39%) in the acupuncture group at 4 weeks • Migraine attacks reduced from 13.6 to 8.9 (33.5%) in the topiramate group at 12 weeks • MIDAS score reduced more significantly in the acupuncture group (81.9%) versus topiramate (71.6%), *p=0.02*

Yang et al 2011 [28]	Acu 33 Drug 33	• Randomized • 24 acupuncture sessions in 12 weeks; no follow up • **Topiramate** 25mg/day increasing by 25mg weekly until 100mg/day then maintenance for 8 weeks • Outcomes: Number of migraine days of moderate/ severe intensity or any severity requiring triptan/ergot MIDAS SF-36	• Migraine days of moderate/severe intensity reduced more significantly in the acupuncture group (20.2±1.5 to 9.8±2.8) versus topiramate group (19.8±1.7 to 12.0±4.1), *p<0.01* • Significantly better improvement with MIDAS with acupuncture versus topiramate (-38.5±10.7 versus -25.9±9.3, respectively), *p<0.01* • Significantly better scores in SF-36 with acupuncture versus topiramate
Ferro et al 2012 [29]	Acu 22 TAN 23 Acu+TAN 23	• Randomized, women only • 20 acupuncture sessions in 10 weeks; no follow up • **Tanacetum** 150mg/day • Outcomes: QoL (SF-36) Score MIDAS VAS score	• QoL (SF-36) scores more significantly improved with acupuncture + Tanacetum, compared to acupuncture or Tanacetum alone • MIDAS scores more significantly reduced in acupuncture + Tanacetum (-42.5±9.8) compared to acupuncture alone (-35.1±10.6) or Tanacetum alone (-24.8 ±11.7), *p=0.025* • VAS scores more significantly reduced in acupuncture + Tanacetum (-6.4±3.1) compared to acupuncture alone (-5.6±2.4) or Tanacetum alone (-3.7±2.1), *p=0.021*
Naderinabi et al 2017 [25]	Acu 50 Botox 50 Control 50	• Randomized • 30 acupuncture sessions in 60 days; follow up 3 months • **Valproate** 500mg/day • Botulinum toxin as per PREEMPT trial protocol • Outcomes: VAS score Reduction in headache days Number of times needing medication	• Comparing groups, VAS scores reduced more with acupuncture at 3 month follow up (*p=0.0001*) • The mean number of headache days at 3 months reduced in acupuncture group from 21.4 to 8.0, in valproate group from 19.1 to 13.1 and in botulinum toxin group from 23.6 to 13.1 • Comparing groups, headache day reduction more with acupuncture at 3 months follow up (*p=0.0001*) • Comparing groups, number of times needing medication reduced more with acupuncture at 3 months follow up (*p=0.0001*)

Acu: Acupuncture; VAS: Visual analogue scale; TAN: Tanacetum; SF-36: Short-Form 36; MIDAS: Migraine Disability Assessment

2.3 Conclusion for Migraine

Taken together, there is some evidence from the Cochrane review [3] and other studies described in this chapter that acupuncture may be effective for episodic migraine. The effects appear to be small and follow up is short (less than 1 year) in most studies. There is perhaps not enough evidence to make any firm conclusions in chronic migraine. It is worth noting that the method of acupuncture administration, sham design and drug administration varies across trials (**Tables 1-4**) which may make direct comparisons unreliable.

It has been suggested that electrostimulation used in two trials [12,20] may be more effective in migraine than manual stimulation used in traditional acupuncture [30]. Another novel trial injected Botulinum toxin at acupuncture points and found this to be more effective at treating migraines than injection of Botulinum toxin at standard sites [31]. More research is needed to validate these methods.

3. Tension Type Headache

A Cochrane review evaluated the use of acupuncture in tension type headache [4] which was again an update on an earlier review [32]. A total of 12 studies were included in their analysis. Like with migraine, the analysis was divided into acupuncture versus sham and acupuncture versus other treatments.

3. 1 Acupuncture versus Sham Acupuncture

In the Cochrane review [4], 5 trials were used to evaluate the difference in reducing headache days between acupuncture versus sham [33-37] (**Table 5**). Acupuncture was statistically superior to sham for reducing the number of headache days at 2 months (mean difference -1.49 (-2.58 to -0.39, p=0.008), 3 to 4 months (mean difference -1.62 (-2.69 to -0.54, p=0.003) and 5 to 6 months after randomization (mean difference -1.51 (-2.59 to -0.43, p=0.006). There was no data for after 6 months.

In the same review [4], the 50% responder rate was superior in acupuncture at 2 months with risk ratio of 1.26 (1.10 to 1.45, p= 0.0008), at 3 to 4 months with risk ratio of 1.27 (1.09 to 1.48, p=0.003) and at 5 to 6 months with risk ratio of 1.17 (1.02 to 1.35, p=0.002). There was no significant difference over 6 months although this analysis was limited to 1 study with only 30 subjects in total [37]. Other investigators aim to provide evidence for the long term effect of acupuncture in tension type headaches in the future [38].

Table 5: A table to show some of the studies comparing acupuncture versus sham acupuncture in tension type headache.

Study	n	Methodology	Results
Yang et 2009 [27]	Acu 12 Drug 12	• Randomized • 24 acupuncture sessions in 12 weeks; no follow up • **Topiramate** 25mg/day increasing by 25mg weekly until 100mg/day then maintenance for 8 weeks • Outcomes: Reduction in migraine days Reduction in migraine attacks MIDAS	• Migraine days reduced from 22.2 to 12.8 (40.1%) in the acupuncture group versus 22.7 to 13.8 (37.8%) in the topiramate group • Migraine attacks reduced from 13.3 to 8.0 (39%) in the acupuncture group at 4 weeks • Migraine attacks reduced from 13.6 to 8.9 (33.5%) in the topiramate group at 12 weeks • MIDAS score reduced more significantly in the acupuncture group (81.9%) versus topiramate (71.6%), *p=0.02*
Yang et al 2011 [28]	Acu 33 Drug 33	• Randomized • 24 acupuncture sessions in 12 weeks; no follow up • **Topiramate** 25mg/day increasing by 25mg weekly until 100mg/day then maintenance for 8 weeks • Outcomes: Number of migraine days of moderate/severe intensity or any severity requiring triptan/ergot MIDAS SF-36	• Migraine days of moderate/severe intensity reduced more significantly in the acupuncture group (20.2±1.5 to 9.8±2.8) versus topiramate group (19.8±1.7 to 12.0±4.1), *p<0.01* • Significantly better improvement with MIDAS with acupuncture versus topiramate (-38.5±10.7 versus -25.9±9.3, respectively), *p<0.01* • Significantly better scores in SF-36 with acupuncture versus topiramate
Ferro et al 2012 [29]	Acu 22 TAN 23 Acu+TAN 23	• Randomized, women only • 20 acupuncture sessions in 10 weeks; no follow up • **Tanacetum** 150mg/day • Outcomes: QoL (SF-36) Score MIDAS VAS score	• QoL (SF-36) scores more significantly improved with acupuncture + Tanacetum, compared to acupuncture or Tanacetum alone • MIDAS scores more significantly reduced in acupuncture + Tanacetum (-42.5±9.8) compared to acupuncture alone (-35.1±10.6) or Tanacetum alone (-24.8 ±11.7), *p=0.025* • VAS scores more significantly reduced in acupuncture + Tanacetum (-6.4±3.1) compared to acupuncture alone (-5.6±2.4) or Tanacetum alone (-3.7±2.1), *p=0.021*
Naderinabi et al 2017 [25]	Acu 50 Botox 50 Control 50	• Randomized • 30 acupuncture sessions in 60 days; follow up 3 months • **Valproate** 500mg/day • Botulinum toxin as per PREEMPT trial protocol • Outcomes: VAS score Reduction in headache days Number of times needing medication	• Comparing groups, VAS scores reduced more with acupuncture at 3 month follow up (*p=0.0001*) • The mean number of headache days at 3 months reduced in acupuncture group from 21.4 to 8.0, in valproate group from 19.1 to 13.1 and in botulinum toxin group from 23.6 to 13.1 • Comparing groups, headache day reduction more with acupuncture at 3 months follow up (*p=0.0001*) • Comparing groups, number of times needing medication reduced more with acupuncture at 3 months follow up (*p=0.0001*)

Acu: Acupuncture; VAS: Visual analogue scale

3. 2 Acupuncture versus routine care/acute treatment only

In the Cochrane review [4], only 2 trials [11,35] were included in their evaluation for acupuncture versus routine care/acute treatment only. The 2 trials were not pooled together for analysis, due to differences in methodology and baseline characteristics [4]. The differences in the number of headache days and 50% responder rates were superior in acupuncture versus control for both studies (details for Jena et al. 2008 in Table 1, Melchart et al. 2005 in Table 4).

3. 3 Conclusion for Tension Type Headache

There is some evidence that acupuncture is superior to sham or routine care/acute treatment in the treatment of tension type headaches but the notable limitations are that evidence is for less than 12 months and that the comparison with routine care is limited to 2 trials [4].

4. Other Headache Disorders

In cluster headache, there have been a few case reports on the effect of acupuncture [39-41]. It has been suggested that perhaps the selection of specific acupuncture points is important [41]. While these case reports show a favorable outcome with acupuncture, further studies are required before any firm conclusions can be drawn.

In trigeminal neuralgia, a 3 armed trial compared acupuncture with sham acupuncture and carbamazepine before, immediately after and 6 months after treatment [42]. This study found that both acupuncture and sham acupuncture reduced headache intensity (visual analogue scale) at 6 months compared to no treatment. However there have been some concerns raised about the methodology in this study [43]. A report of 12 cases [44] which did not respond to conventional therapy showed a significant improvement with acupuncture therapy in headache intensity (visual analogue scale). A proportion of patients 5/12 remained in complete remission for 11 to 15 months following last acupuncture treatment [44]. Another recent systematic review included 33 randomized controlled trials and found that acupuncture (and electro acupuncture) may be effective for trigeminal neuralgia, although the level of evidence was low [45].

5. Discussion

There is growing evidence in the literature regarding the use of acupuncture in headache disorders. Most of these studies are on the treatment of migraine and tension type headache, which are the two most common primary headache disorders. The Cochrane reviews indicate that acupuncture may be effective for these conditions, although the effects may be small [3,4].

The Cochrane reviews also provide evidence that acupuncture is generally safe and well

tolerated. In the acupuncture versus sham acupuncture analysis dropouts due to adverse effects were 0% versus 0.5%, respectively and in the acupuncture versus prophylactic drug treatment analysis, dropouts due to adverse effects were estimated to be 2% and 7.1% respectively [3]. In terms of rates of adverse effects reported (per participant), they were similar in acupuncture versus sham analyses (estimated 19.9% versus 17.3%, respectively) but consistently fewer adverse effects reported in acupuncture in studies comparing to prophylactic drug treatment analyses (estimated 11.4% versus 34.1%, respectively) [3]. Similar results were found in the Cochrane review for acupuncture in tension type headache [4]. A separate group reviewed the safety and tolerability of acupuncture in pregnancy, although the reviews were not limited to headache disorders [46]. The total adverse effect incidence (per acupuncture session) was estimated at 1.3% after excluding those not felt to be directly caused by the acupuncture treatment [46]. The authors found the most commonly reported mild/moderate adverse effects included pain, bleeding/bruising, worsening of symptoms, hypotension, syncope, rash and tiredness. The serious yet rare adverse effects included infection, nerve damage and pneumothorax. Other serious reported adverse effects such as hypertension/pre-eclampsia and congenital defects were felt to be unlikely caused by the acupuncture treatment [46]. The reported miscarriage rate in the review was actually lower than the population risk suggesting there is no increased risk with acupuncture [46]. Taking these results together, acupuncture appears to be a relatively safe and well tolerated option, possibly even in pregnancy.

A few studies have assessed the cost effectiveness of acupuncture in headache disorders. A 2018 Czech study evaluated the economic costs of adjuvant acupuncture to pharmacological treatment versus pharmacological treatment alone in migraine patients [47]. The assessment considered the perspectives of paying third party, patient and societal costs. The total costs (which were not statistically different) were estimated at €691.1 versus €284.7 (p=0.26) after 3 months of acupuncture and €65.7 versus €131.9 (p=0.07) after 6 month follow up, for acupuncture and control respectively [47]. Within these figures, productivity and income losses were lower with the acupuncture group but this was not statistically significant. A study based on UK primary care in 20004 assessed the cost effectiveness of 12 sessions of acupuncture (over three months) in comparison to usual care [48]. They found that there is an average gain of 0.021 quality adjusted life years (QALYs) but with a mean increased cost of £403 in the acupuncture group versus £217 for the usual care group. This results in £9180 per QALY gained and the analysis predicts that the cost per QALY may be lower for subsequent years [48]. A German study in 2008 compared acupuncture to routine care in patients with headaches found that the incremental cost-effectiveness ratio (ICER) was €11,657 [49]. The results of these 2 studies need to be interpreted with caution as the cost analyses are over 10 years old.

In summary, acupuncture is a possible safe and relatively well tolerated option in patients who have tried conventional oral therapy for migraine and tension type headaches and its use is currently supported by NICE in the UK.

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