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The effectiveness of acupuncture in the management of persistent regional myofascial head and neck pain: A systematic review and meta-analysis

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ABSTRACT

Persistent head and neck myofascial pain is among the most frequently reported pain complaints featuring major variability in treatment approaches and perception of improvement. Acupuncture is one of the least invasive complimentary modalities that can optimize conventional treatment. The aim of this review was to determine the evidence for the effectiveness of acupuncture in the management of localized persistent myofascial head and neck pain. Only randomized controlled clinical trials (RCTs) were included. The search was conducted in PubMed, Ovid Medline, Embase, Google Scholar, and Cochrane Library in addition to manual search. The main outcome measure was the comparison of the mean pain intensity score on VAS between acupuncture and sham-needling/no intervention groups. Safety data and adherence rate were also investigated. Six RCTs were identified with variable risk of bias. All included studies reported reduction in VAS pain intensity scores in the groups receiving acupuncture when compared to sham needling/no intervention. Meta-analysis, using a weighted mean difference as the effect estimate, included only 4 RCTs, revealed a 19.04 point difference in pain intensity between acupuncture and sham-needling/no intervention (95 %CI: -29.13 to -8.95). High levels of safety were demonstrated by the low rates of side effects/withdrawal. Inconsistency in reporting of outcomes was a major limitation. In conclusion, moderate-quality evidence suggests that acupuncture may be an effective and safe method in relieving persistent head and neck myofascial pain. Optimizing study designs and standardizing outcome measures are needed for future RCTs.

1. Introduction

Head and neck myofascial pain is defined as pain originating in the muscles of the head and neck area that is affected by local function and/or parafunction, and can be replicated by provoking the offending muscle.[1] It can be associated with trigger points, a hyperirritable nodule in a taut band of skeletal muscle, generating spontaneous or triggered pain that can be confined to the affected muscle or spreads and refers to the adjacent structures.[2,3] Head and neck myofascial pain is among the common chronic health complaints in the general population.[4,5] Collectively with other temporomandibular joint disorders (TMDs), the condition can affect up to 12 % of the US population, with an estimated annual healthcare cost of $4 billion.[6]

Symptoms of head and neck myofascial pain may vary from mild intermittent discomfort to severely disabling pain and dysfunction that may negatively affect the patient's quality of life.[7] In western medicine, several treatment modalities are available with variable levels of success, inconsistent outcomes, and non-negligible side effects.[8–12] Acupuncture, including trigger point dry needling techniques, may represent a good adjuvant method to treat refractory cases. It can also be used as an alternative option in case of failure or contraindication of the conventional western treatment modalities.[13,14]

Several murine model investigations have been conducted to uncover the underlying physiologic effect of acupuncture. Analgesia, in specific, was one of the largely investigated aspects in which several mechanisms of action were postulated. Modification of N-methyl-D-aspartate (NMDA) receptor signaling pathway in the spinal cord,[15] reduction of the proinflammtory cytokines levels in both peripheral nerves and dorsal root ganglia,[16] and activation of p38MAPK in spinal dorsal horn[17] are among the likely mechanisms of action. Shah et al. investigated the *in vivo* biochemical changes associated with myofascial trigger point needling in the human model and reported an immediate drop in neuropeptides (substance P and calcitonin gene related protein) after needling.[18]

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In 1997, the National Institutes of Health (NIH) consensus statement on acupuncture came in support of the efficacy of acupuncture in treating pain and nausea.[19] Since then, the utilization of acupuncture has steadily increased. In 2007, the US National Health Interview Survey (NHIS) reported that over 3 million adults in the US had used acupuncture in the previous year (10 % of the total population).[20] "Despite the growing recognition and utilization of acupuncture, the supporting evidence for its effectiveness is still lacking. This can be correlated to the methodological flaws in some of the previously conducted clinical trials with inadequate and/or heterogenous criteria of inclusion, control arm, randomization of participants, assessment of outcome measures, and length of follow up. Consequently, conduction of systematic reviews concerning the effectiveness acupuncture in regional persistent head and neck myofascial pain has been very limited and drawing clinically meaningful conclusions has been difficult to achieve.[21,22]"

The aim of this systematic review is to critically review all published randomized clinical trials concerning the effectiveness of acupuncture in the management of localized persistent myofascial pain in the head and neck region.

2. Materials and methods

2.1. Protocol registration

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines.[23] The protocol for this systematic review was registered at the International prospective register of systematic reviews (PROSPERO), University of York Center for Review and Disseminations. The protocol can be accessed through http://www.crd.york.ac.uk/PROSPERO with registration number CRD42016042956.

2.1.1. Data items

To answer the question regarding the effectiveness of acupuncture in managing persistent myofascial pain in the head and neck region the following PICO question was formulated. **Population:** patient with persistent regional head and neck myofascial pain; **Intervention:** acupuncture including trigger point dry needling; **Comparison group:** placebo defined as people receiving sham acupuncture (no needle penetration) or no intervention at all (e.g. waiting list group); **Outcomes:** 1) primary outcome: reduction in the mean pain intensity score reflected on VAS or other similar numeric or descriptive scales at short-term follow up (i.e. at or within 1 weeks after finishing the acupuncture sessions) and long-term follow up (i.e. 1 month or beyond after finishing the acupuncture sessions),2) secondary outcome: The Short Form Health Survey (SF-36) which is a self-administered quality-of-life measures for assessment of care outcomes in adult patients[24] (not reported in all studies). For simplification of the outcome measures the Neck pain and disability scale" (NPDS), reported in the study by Witt et al., was considered analogous to VAS pain intensity.

2.2. Eligibility criteria

Inclusion criteria included; randomized clinical trials, population of myofascial pain limited to the head and neck area, persistent pain of 30 days or more, traditional Chinese/Japanese acupuncture including trigger point dry needling technique, adequate number of treatment sessions (not less than 5 sessions), adequate length of follow up (at or within the first week after the end of treatment (EOT)), trials reporting subjective mean pain intensity scores on VAS, or other similar scales, as an outcome measure.

Criteria for exclusion included; non English literature, irrelevant intervention (not acupuncture or dry needling), irrelevant population (patient who don't have regional neck/head/face/TMJ myofascial pain), trials that are non-randomized, trials lacking the control arm, trials concerning other chronic pain conditions (back pain and neuropathic pain) and/or widespread pain disorders (e.g. fibromyalgia, spinal cord injury, etc..) and/or systemic disease such as rheumatoid arthritis where population with regional head and neck myofascial pain cannot be separated, and publications not available in full text.

To eliminate possibility of faulty results, all control groups that are not "true placebo" (true placebo is defined as sham needling with no skin penetration) or "no treatment" were not considered in the analysis of this systematic review. Moreover, comparison groups that received any other interventional treatment modalities (e.g. message or splint therapy) were also excluded from the analysis.

2.3. Information sources and search strategy

A systematic search of the medical literature was performed during June of 2019 to identify all clinical trials concerning the effectiveness of acupuncture in treating persistent regional myofascial pain of the head and neck. The main author (AF) received assistance from Tufts University librarians (ER, AL, AN) to initiate the search strategy. The search was conducted in the National Library of Medicine (PubMed), Ovid Medline, Embase (via Scopus), Google Scholar, and Cochrane Library (please refer to Appendix 1 for detailed search strategy). The yield was further supplemented by a manual search of the literature, which consisted of creating a reference list of the selected papers, as well as the most recent (2013+) systematic reviews concerning this topic.

Search terms used were; Acupuncture, analgesia, acupuncture therapy, acupuncture, head pain, neck pain, facial pain, myofascial pain syndromes, chronic pain, and nociceptive pain. The search was restricted to randomized clinical trials. Detailed search strategy can be viewed by accessing the following link:

https://www.scribd.com/document/417893626/Appendix-1-Search-Strategy.

2.4. Studies selection and data extraction process

Two authors (AF and AM) independently performed assessment for the papers eligibility by screening the titles. Selected papers were further assessed by reading the abstracts and the final list of papers was agreed upon. A third author (GM) resolved any disagreement in regard to papers selection. Full text review, assessment of the studies' quality, and data extraction were performed by the same two authors (AF and AM). The third author (GM) carefully reviewed the extracted data to minimize any chance of error, interpersonal variability, and personal bias. For any missing data, authors of the included studies were contacted by e-mail and asked to provide the specific data needed.

2.4.1. Risk of Bias and quality assessment of randomized clinical trials

Risk of bias assessment within and across the included RCTs was performed using the Cochrane Risk of Bias tool.[25] The following six domains were evaluated: 1) selection bias (random sequence generation, allocation concealment); 2) performance bias (blinding of participants and personnel); 3) detection bias (blinding of outcome assessment); 4) attrition bias (incomplete outcome data); 5) reporting bias (selective reporting); and 6) other bias.

2.4.2. Summary measures and synthesis of results

Meta-analysis was conducted using Stata Version 13.1 (StataCorp LLC, College Station, TX). The meta-analysis was reported according to the QUOROM (Quality of reporting of meta-analysis) guide-lines.[26] Effect size was measured with standardized mean difference (SMD). A meta-analysis for the outcome of pain intensity was performed using a random effects model. Heterogeneity was assessed visually with a forest plot and with Cochran's Q test and the I^2 statistic.[27] A meta-regression was used to investigate potential sources of heterogeneity. A contour-enhanced funnel plot was visually evaluated for publication bias;

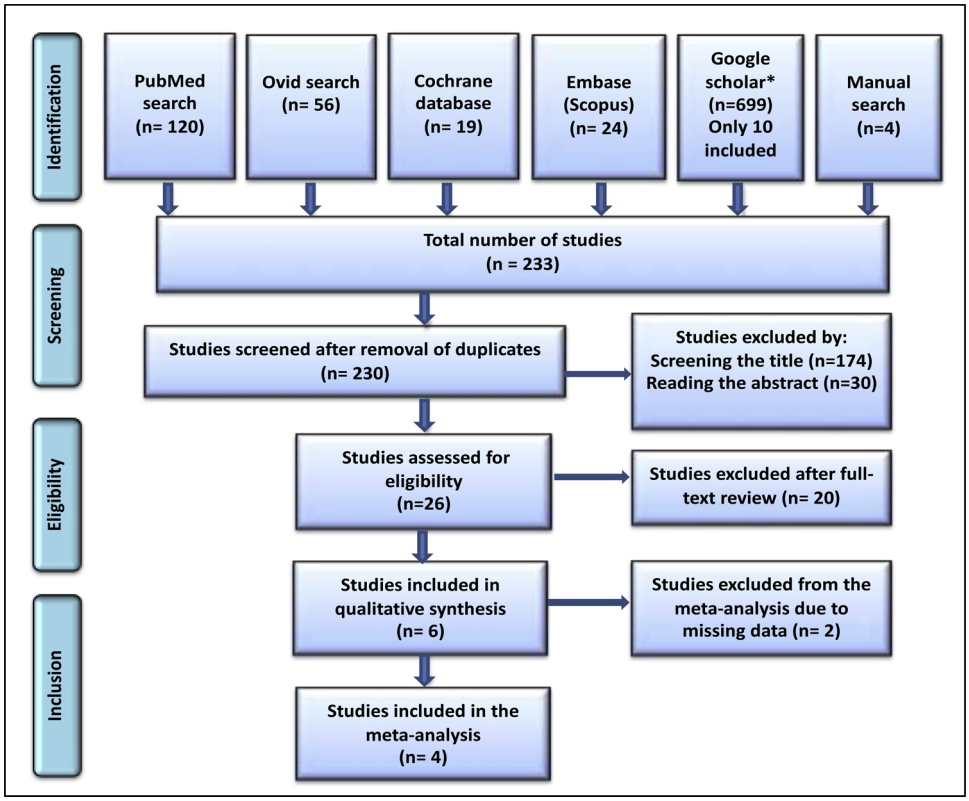

Fig. 1. Search strategy and paper selection.
*Google search yielded 699 paper. Only 10 were deemed relevant and were included in the screening stage.

publication bias was further determined using Egger's linear regression test and the Begg-Majumdar rank correlation test.

3. Results

3.1. Study selection

A total of 964 papers were identified through the search, of which, 734 were excluded due to irrelevance or duplication. Two hundred and thirty papers proceeded to the screening stage and 204 papers were eliminated after screening the titles (n = 174) or reading the abstracts (n = 30). Upon careful review of the full texts of the remaining 26 papers, a total of 6 papers were deemed eligible for this systematic review (Fig. 1).

3.1.1. Risk of Bias within and across the studies

The Cochrane Risk of Bias tool demonstrated some degree of bias among each individual study with Johansson et al. being the one with the highest risk of bias and Irnich et al. having the lowest risk (Fig. 2).[28] Across the studies, 4 out of the 6 studies have high-risk of detection bias, 2 out of 6 have high risk of reporting biases as well as other biases, and one study has high risk of attrition bias (Fig. 3). Four out of the 6 studies have unclear risk of selection bias (Fig. 3).

3.2. Study characteristics

The 6 randomized clinical trials were published between 1991 and 2006. The number of study participants in each study varied between 16 and 14,161. The number of treatment sessions ranged from 5 to 14 with the majority of the sessions lasting 30 min. Table 1 includes the details for the characteristics of the studies.

3.3. Results of individual studies

3.3.1. Primary outcome

All included RCT reported pain intensity on VAS as an outcome measure except for the study by Witt et al. in which "Neck pain and disability scale" (NPDS) was the main outcome measure. For simplification purposes, NPDS was considered the primary outcome, since VAS is one of the components of the NPDS, and was used for comparison with the primary outcomes of the rest of the studies.

At short-term follow up, all the included studies reported reduction in pain intensity after treatment. Statically significant improvement was reported in the acupuncture group compared to placebo in 4 studies [Birch et al. ($p < 0.05$); Itoh et al. ($p = 0.003$); List et al. ($p < 0.01$); Witt et al. ($p < 0.001$)].[29–32] No statically significant difference between acupuncture and placebo was found in Irnich et al. study ($p = 0.388$).[33] No statistical conclusion can be drawn from Johansson et al. study as the p-value was not reported.[28] Table 2 summarizes the results of the primary outcome of each study.

At long-term follow up, statically significant improvement was reported in the acupuncture group compared to placebo in 3 studies [Birch et al. ($p < 0.05$); Johansson et al. ($p < 0.01$); Witt et al. ($p < 0.006$)].[28,29,31] However, no statically significant difference between acupuncture and placebo was found in Irnich et al. study ($p = 0.388$).[33] No statistical conclusions can be drawn from Itoh et al. and List et al. studies due to the lack of reporting of p-values (Table 2).[30,32]

3.3.2. Secondary outcomes

Secondary outcomes were not consistent among the studies. Short-Form Health Survey (SF-36) was the most commonly reported (used in 3 studies).[29,31,33] Pressure pain threshold was reported in 2 of the studies,[30,33] active range of motion was reported in 2 studies (neck range of motion[33] and jaw range of motion[32]), and Clinical dysfunction

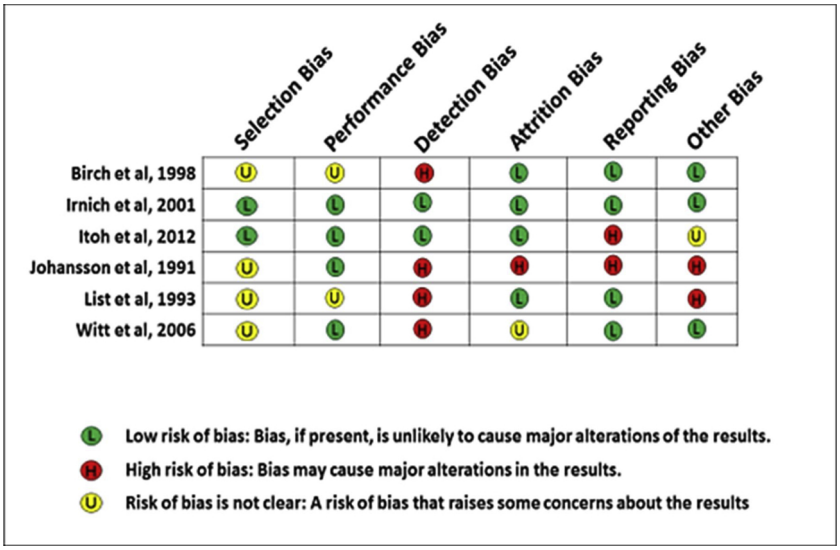

Fig. 2. Cochran Risk of Bias assessment for individual studies.

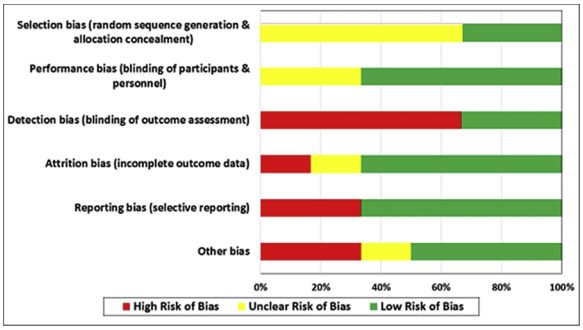

Fig. 3. Cochran Risk of Bias assessment across the studies.

score was reported by 2 studies.[28,30] In this investigation, SF-36 was considered the main secondary outcome. Birch et al. reported no statistical differences in pre- and post-treatment SF-36 scores between acupuncture and control groups (numbers not provided).[29] Irnich et al. limited the reporting of SF-36 to the most significant components (role physical and pain index).[33] At the end-of treatment visit, there were no statistical differences between the acupuncture and the sham laser group in both components [role physical ($p = 0.498$) and pain index ($p = 0.989$)]. Similarly, no differences detected at 3-month follow up on both parameters (role physical: $p = 0.825$; pain index: $p = 0.870$).

Witt et al., found no statistically significant differences at baseline score between randomized acupuncture and control groups in all components of the SF-36 (p-values ranges between 0.058 and 0.490) except for bodily pain ($p < 0.001$).[31] At 3-month follow up, the percentages of reduction in the SF-36 scores (all component) were significantly higher in the randomized acupuncture group in comparison to controls ($p < 0.001$).[31]

3.3.3. Withdrawal rate and reasons for withdrawal

Four out of the six studies reported withdrawal rate.[29,30,32,33] The calculated percentage of withdrawal in the intervention groups ranged between 0 % (List et al) and 26 % (Birch et al) while a smaller rate was observed in the controls (0 %–20 %).[29,30] Side effects and reasons for withdrawal is summarized in Table 3. Calculating the rate of withdrawal in the study by Witt et al. was not feasible due to the lack of disclosure of number of withdrawing subjects. Percentages of side effects (reasons for withdrawal) were reported after combining data form both randomized and non-randomized groups (non-randomized group was initially excluded from the analysis) which hindered the calculation of the side effects in the randomized group (Table 3).[31]

3.3.4. Synthesis of results

Only one paper reported both mean change from baseline with a corresponding standard deviation (Irnich et al.). In order to calculate a standard deviation for mean change from baseline for the remaining included studies, a correlation coefficient was calculated from the reported change from baseline data from Irnich et al. for both acupuncture (0.485) and sham groups (0.508) as described in the Cochrane Handbook.[27] As the mean correlation coefficient of 0.495 was less than the 0.5 cutoff recommended[27], the meta-analysis was performed with the reported follow-up data rather than the change from baseline for the most precise results.

3.4. Meta-analysis – random effects model

Due to lack of reporting of some primary outcome measures in Johansson et al. study and lack of reporting of mean VAS pain intensity score as a primary outcome measure in Witt et al. study, inclusion of these two RCTs in the meta-analysis was not feasible. Only four out of the six studies were included in the meta-analysis.[29,30,32,33] A random effects model was used to take into account study variances and tau-square (heterogeneity between the studies) and to give smaller studies more weight. Using a weighted mean difference as the effect estimate, the mean VAS pain intensity score in the acupuncture group was 19.04 points less than the sham treatment (95 % CI: -29.13 to -8.95) (Fig. 4).

3.4.1. Level of heterogeneity

An I^2 value of 52 % (95 %CI: 0–84) represents moderate to substantial heterogeneity between the studies (Fig. 4). Given the large confidence interval, the likelihood of substantial heterogeneity is suggested. Although Cochran's Q was not statistically significant ($p = 0.10$), this test has low power with small numbers of studies and thus the results were not strongly considered when analyzing heterogeneity. To explore possible sources of heterogeneity, meta-regression analysis for in-between –studies-variance was conducted. Effect estimates did not vary with sample size ($p = 0.203$), average baseline VAS score ($p = 0.696$), gender ($p = 0.874$), or duration of treatment ($p = 0.158$).

3.4.2. Risk of publication Bias

Publication bias was assessed graphically with a funnel plot. The funnel plot suggests no significant publication bias as the plot is fairly

Table 1
Studies characteristics.

Author	Year of publication	Journal	Duration of pain	Acupuncture technique	No. of sessions	No. of treated points	Regional point
Birch et al[29]	1998	The Clinical Journal of Pain	≥ 6 months	Japanese	14	20	6 bilateral points: GB-20, GB-21, GB-12, BL-10, BL-11, & GV-14 with infrared stimulation
Irnich et al[33]	2001	British Medical Journal	> 1 month	Traditional Chinese	5	NR*	GB-20, SI-14 & myofas cial dry needling
Itoh et al[32]	2012	Journal of Acupuncture and Meridian Studies	≥ 6 months	Trigger point dry needling	5	NR (Depending on patients need)	Myofascial dry needling (average of 4.2 points)
Johansson et al[28]	1991	Acta odontologica Scandinavica	Long-standing	NR	6	4-8	3-7 points (not specified) with manual stimulation
List et al[30]	1993	Journal of orofacial pain	≥ 6 months	NR	6 (except for 6 patients that received 8)	Total of 6	Ex-2, St-7, St-6, & Gb-20 with electrical stimulation
Witt et al[31]	2006	Pain	≥ 6 months	According to the physician preference	10.2 ± 2.4	NR (according to the examiner)	Not specified (according to the, manual stimulation may be used)

Author	Distant point	Control group	Third group excluded	Concurrent use of analgesics	No. of subjects	Male	Female	Age Range (yrs)	Mean age (yrs)
Birch et al[29]	4 bilateral points: SI-3, BL-62, & GB-41 with diod stimulation	No sham only nonintervention controls	Yes, sham needling group due to needle penetration	500 mg Trisilate TID for both intervention and control groups	Total of 46 (30 after exclusion of third group)	4	26	18 - 65	39.75 for the entire study population
Irnich et al[33]	SI-3, UB-10, UB-60, Liv-3, GB-20, GB-34, TE-5, & ear point	Sham acupuncture with inactivated laser pen. Points similar to intervention group	Yes, group receiving message therapy	NR	Total of 177 (117 after exclusion)	38	117	NR	52.4 total (Acupunture =- 52.3 Sham = 52.2)
Itoh et al[32]	None	Needle tips were cut off to prevent penetration. Points similar to intervention group	None	NR	16	11	5	19-24	NR & could not be calculated
Johansson et al[28]	Li 4 with manual stimulation	No sham only nonintervention controls	Yes, group receiving splint therapy	NR	Total of 45 (numbers in each group not reported)	NR	NR	NR	NR

Table 1 (*continued*)

Author	Distant point	Control group	Third group excluded	Concurrent use of analgesics	No. of subjects	Male	Female	Age Range (yrs)	Mean age (yrs)
List et al[30]	Li-4 & St-36	No sham only nonintervention controls	Yes, group receiving splint therapy	NR	Total of 55 (35 after exclusion)	Total of 9 (number after exclusion was not reported)	Total of 46 (number after exclusion was not reported	22-69	Median age; F:43, M:37 for the total study population
Witt et al[31]	NR	No sham only nonintervention controls (Waiting list)	Non-randomized acupuncture group	Regular regimen permitted (regimens not specified)	3451 after exclusion of non-randomized patients) (1753 acupuncture, 1698 control)	1074 (Calculated)	2377 (calculated)	NR	50.6

* NR: Not reported.

symmetrical (Fig. 5). Additionally, both Begg's test ($z = 1.02$, $p = 0.308$) and Egger's test ($p = 0.187$) were not statistically significant; thus there is no evidence of publication bias.

4. Discussion

4.1. Summary of evidence

4.1.1. Primary outcome measures

The primary objective of this systematic review was to determine the effectiveness of acupuncture and dry needling in managing persistent regional head and neck myofascial pain. Six randomized clinical trials met the established criteria and were included in this investigation. To decrease the risk of methodological flaws and confounding factors, the selection of control groups was limited to subjects who received no interventions at all (e.g. waiting list) or those who received sham acupuncture that includes no needle penetration (true placebo).

Overall, positive primary outcome (reduction of VAS pain intensity score or similar scale in acupuncture group compared to controls) was found among all studies.

With no differences in pain levels at baseline, Witt et al. demonstrated significant improvement NPDS scores at the end of treatment for patients receiving acupuncture.[31] They further showed that the intervention group was able to maintain better levels of pain relief even after 6 months of treatment completion compared to no intervention group (all NPDS scores and P values were reported). Birch et al., reported similar findings at baseline, end-of-treatment and long term follow up.[29] Although, the mean VAS scores were not reported in numbers at long term follow-up, p-value and a statement of significant improvement in the acupuncture group was provided in the text of the paper. Itoh et al. demonstrated that, regardless the overall improvement of both acupuncture and sham groups, the acupuncture group had significantly lower pain intensity levels over the observation period using repeated measures analysis.[32] Johansson et al., reported no statistical differences in pain intensity between acupuncture and control groups at baseline.[28] No pain intensity scores were reported at the end-of-treatment but at long-term follow up, significant positive improvement was detected in the intervention group compared to the controls.[28] List et al. reported a statistically significant improvement on the pain intensity scores of the intervention group compared to controls at short term follow up.[30] Unfortunately, no data was reported for long-term follow-up.

Irnich et al. showed that, with no differences in VAS pain intensity scores at baseline, subjects in the intervention group had lower pain levels after receiving treatment compared to their counterparts in the control arm. Although positive findings were reported on both short and long-term follow-ups, this was the only study in which results did not meet statistical significance.

4.1.2. Secondary outcomes measures

The improvement in SF-36 score was reported in only 3 of the six RCTs[29,31,33] with only 2 reporting significant improvement at follow up.[29,31] Drawing conclusion in regard to the improvement of SF-36 is not feasible due to limited number of papers showing efficacy in addition to the lack of reporting of the actual numbers in one of these RCTs.[31]

Side effect and withdrawal rate did not differ majorly between the intervention and control groups in all studies. No major adverse effects were reported. This indicates high level of safety of acupuncture and trigger point dry needling.

4.2. Limitations

4.2.1. Limitations in the studies included in this investigation

A few important points should be mentioned in regard to the results found in some of the RCTs included in this investigation. Language

Table 2
Summary of Primary outcome measures of all the studies.

	No. of subjects		Baseline			Short-term Follow-up				Long-term Follow-up			
			Mean VAS			Time point	Mean VAS			Time point	Mean VAS		
	Intervention	Controls	Intervention	Controls	P-value		Intervention	Controls	P-value		Intervention	Controls	P-value
Birch et al[29]	15	15	48	49	NR*	EOT (10 wks after initiation of tx)	18.7 (SD = 19)	47.6 (SD = 20.5)	< .05	3 months after EOT	NR £	NR £	< .05
Irnich et al[33]	56	61	54.15 (SD = 21.91)	57.15 (SD = 26.71)	NR	At or within the 1st WK after EOT (3 or 4 weeks after TX initiation)	29.93 (SD = 22.6) (calculated)	39.87 (SD = 26.5)	0.388	3 months after EOT	36.75 (SD = 29.7)	39.75 (26.4)	1.000
Itoh et al[32]	7	8	67.1 (SD = 19.1)	65.6 (SD 15.2)	NR	EOT (5 W K after TX initiation)	≈10 **	≈40 **	0.003	5 wk after EOT	≈20 **	≈55 **	NR
Johansson et al[28]	15	15	≈ 55 **	≈ 52 **	NR ¥	NR	NR	NR	NR	3 & 2 months after baseline visit	≈ 30 **	≈ 60 **	p < 0.01
List et al[30]	20 (At the 6 months follow-up only 14 patients evaluated)	9	18 (SD = 11)	30 (SD = 17)	NR ¥	EOT (6–8 W K after TX initiation)	12 (SD = 7)	29 (SD = 19)	< 0.01	6months (not clear if after TX initiation or EOT)	NR	NR	NR
Witt et al §[31]	1753	1698	55.0 (SD = 15.8) NPDS not VAS §	53.9 (SD = 16) NPDS Not VAS §	0.056	EOT (at 3 months after TX initiation)	NPDS reduction = 28.9 % (NPDS = 39.1 calculated) (95% CI-27.6; 30.2)	NPDS reduction = 5.8 % (NPDS = 50.8 calculated) (95% CI-4.5;7.1)	< 0.001	3 months after EOT	NPDS reduction = 28.0 % (NPDS = 39.6 CALCULATED) (95% CI-26.5; 29.4)	NPDS reduction = 25.1 % (NPDS = 40.4 calculated)(95%CI-23.6; 26.5)	0.006

EOT: End of treatment; WK: weeks; TX: treatment.
*NR: Not reported.
¥ P value was not reported but it was stated in the text that no statistically significant difference was found between the acupuncture and control groups.
£ Numbers not reported. Authors stated that acupuncture group has significant reduction in mean VAS pain score compared to controls.
** Numbers for mean VAS pain score are not reported; approximate mean VAS was obtained from the provided Bar charts.
NPDS: Neck Pain Disability Scale.
§The study by Witt et al used NPDS as a primary outcome measure; VAS is one of the components of this Scale.

Table 3
Withdrawal rate and reasons for withdrawal.

Author	Intervention group		Control group	
	Number of withdrawals (%)	Reasons for withdrawal	Number of withdrawals (100 %)	Reason for withdrawal
Birch et al[29]	4 out 15 (26 %)	Moved, drop-out, lost contact (exact numbers not specified)	3 out of 15 (20 %)	Moved, drop-out, lost contact (exact numbers not specified)
Irnich et al[33]	7 out of 56 (12.5 %)	Withdrew from trial = 1; Refused acupuncture = 1; Had accident = 1; Diagnosed with nerve root compression = 1; Lost to follow-up = 3	4 out of 61 (6.56 %)	Withdrew from trial = 2; Diagnosed with infectious disease = 1; Lost to follow up = 1
Itoh et al[32]	1 out of 7 (14.3 %)	Worsening symptoms = 1	0 out of 8 (0 %)	————
Johansson et al[28]	Not specified	Not specified	Not specified	Not specified
List et al[30]	0 out of 20 (0 %)	————	0 out of 9 (0 %)	————
Witt et al[31]	Difficult to track as some patients did not complete questionnaires	1,005 out of 11,288 patients in both randomized and non-randomized groups reported side effects (8.9 %); 57 % minor bleeding or hematoma, 10 % pain, 4 % vegetative symptoms & 29 % other	Not reported	Not reported

Fig. 4. Forest Plot demonstrating the level of heterogeneity and effect estimate.

Fig. 5. Funnel plot demonstrating the risk of publication bias.

restriction lead to exclusion of several, and presumably good, RCTs published in Chinese or Japanese languages. However, translation of these RCTs was unfeasible due to the huge number of papers that may require language translation and the lack of fund to cover such expenses.

Major variability in the reported outcome measures and follow up timeline were observed when the RCTs were reviewed. The lack of reporting of the raw data (numbers) was also one major obstacle that hindered the inclusion of some studies in the meta-analysis.

Itoh et al. and Johansson et al. did not report the actual numbers for VAS pain intensity score at short and long-term follow-ups.[32] Alternatively, numbers were estimated by looking at the graphs provided in the paper. The absence of the actual numbers for VAS pain intensity score is a major factor that sub-optimized the accuracy of the reported results. In addition, p-values were not reported for the differences in VAS pain intensity scores between intervention and control groups at short-term follow-up on both studies and on long-term follow-up in Itoh et al. study. This compromised the ability for drawing accurate conclusions.

In the study by Irnich et al.,[33] there was no mention of the p-value at the baseline mean VAS pain intensity score but the reported scores on both intervention and control groups did not differ majorly. On the other hand, List et al. study had a major difference in baseline mean VAS pain intensity score in the control group (30 out of 100) compared to the intervention group (18 out of 100) with no reporting of the p-value that should be insignificant prior to any intervention. Major differences in baseline mean VAS score between the comparison groups contribute to inaccuracy of outcomes.

4.2.2. Limitations detected in the literature overall

Generally, several studies suffered some methodological and study design flows that might affect the integrity of the study outcomes and led to exclusion from this investigation.

1 Heterogeneity of study population and broad subjects selection criteria: the huge diversity in the diagnoses of the study populations (e.g. osteoarthritis pain, spinal cord pathology, and fibromyalgia) was one of the challenges encountered during study selection.
2 Heterogeneous intervention techniques: great variability was detected in terms of acupuncture techniques, needling points, numbers and length of sessions.
3 Lack of true placebo control group: studies using sham acupuncture that includes needle penetration repeatedly appeared during this review. Skin penetration can stimulate the effect of acupuncture even if too shallow it is thought to be off meridian (away from the acupuncture point). This can be mainly due to anatomical variation between individuals that may consequently induce changes in proinflammatory cytokines production and receptors signaling pathway in the spinal cord. [15,16]
4 Lack of reporting of concurrent medications that can be a major modifying effect of the intervention outcomes.
5 Lack of standardization of short and long-term follow-ups.

It is understandable that, with contemporary study methodologies, this risk can be minimized but cannot be completely eliminated due to the infeasibility of double blinding in these kind of studies (i.e. acupuncturist cannot be blinded).

4.3. Summary of finding from the meta-analysis

Although the meta-analysis showed moderate evidence in regard to the effectiveness of acupuncture, compared to controls, in managing persistent regional myofascial pain of the head and neck region, several points must be taken into consideration:

1 Evidence of effectiveness might be limited due to the few number of studies, the smaller sample sizes in each study, and the wide spread of the 95 % confidence interval of all the included studies (although no intersection with null was found).
2 The high level of heterogeneity between the included studies may also compromise the level of evidence and make it questionable.

5. Conclusions and future directions

There is moderate evidence of the effectiveness of acupuncture in managing persistent regional myofascial pain in the head and neck region. However, finding from the meta-analysis may question this conclusion. Safety data is very encouraging with absence of serious adverse events and low withdrawal rate. No conclusion can be drawn regarding the improvement of SF-36 due to limited evidence.

Generally, there is an obvious necessity for a higher level of standardization in the methodology and the outcome measures reporting among RCTs in order to provide stronger evidence for the effectiveness of acupuncture. It is the hope that this review can assist in providing a summary for the factors that should be taken into consideration when designing future studies to enrich the literature and facilitate the conduction of higher quality systematic reviews and meta-analysis.

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Declaration of Competing Interest

None to declare.

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