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LETTER

Interpreting the Evidence for Laser Acupuncture in Knee Osteoarthritis Management: A Call for Methodological Rigor and Nuance [Letter]

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Dear editor

Pain is a primary reason for individuals to seek acupuncture treatment.[1] Laser acupuncture (LA), which preserves the conceptual foundations of acupuncture while being non-invasive,[2] garners increasing research attention as a potential modality for pain management. A recent systematic review and meta-analysis (SR/MA) by Zeng et al evaluates the analgesic efficacy of LA for knee osteoarthritis (KOA).[3] While their work contributes valuable clinical evidence, we have methodological concerns and hold differing perspectives on certain aspects of the study. We welcome the opportunity to further discuss these issues with the authors.

Accuracy Considerations in Trial Reporting and Interpretation

First, Zeng et al's SR/MA incorporates five randomized controlled trials (RCTs).[3] In their results, the authors state that "Two trials were conducted in China,[4,5] and the remaining ones in Australia,[6] the UK,[7] and India".[8] However, verification shows that the trial attributed to the UK is actually conducted at the Security Forces Hospital in Saudi Arabia,[7] and the trial ascribed to India is performed at Cipto Mangunkusumo Hospital in Indonesia.[8]

Second, an inaccuracy pertains to the "Length of Follow-Up" presented in Table 1 of the aforementioned SR/MA. Re-examination of the original RCTs indicates that the reported values likely correspond to the intervention periods rather than follow-up durations. To enhance precision and clinical relevance, both the intervention and follow-up periods of the included studies are recompiled (see our Table 1).

Third, in the same table, the intervention modality of the 2014 RCT by Al Rashoud et al[7] is described as "Laser & Exercise versus Exercise and Exercise." In reality, the intervention group receives LA combined with straight leg raise exercises and supportive health education/advice for coping with KOA, whereas the control group underwent the same exercise and education/advice protocol along with placebo-LA (see our Table 1).

Finally, a notable inconsistency exists between the statements in the "Overall Findings" and "Conclusion" sections. The former states that LA has "little to no effect" compared to exercise therapy, while the latter concludes that patients undergoing LA "may experience a greater reduction in pain intensity." This interpretation appears primarily based on a single trial,[5] in which the between-group difference [WMD −0.84 cm, 95% CI (−1.12 to −0.56)] does not exceed the pre-specified 1 cm minimal important difference (MID) in Visual Analogue Scale. We respectfully caution against an overly rigid application of the MID in this context, as its clinical relevance can vary based on population, baseline severity, and, notably, the choice of comparator.[9] Given that exercise itself is an effective, guideline-recommended

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Table 1 Re-Extraction of Characteristics from the Five RCTs Included in Zeng et al's Study

Trials	Study Location	Interventions		Controls	Follow-Up Period
		Modality	Dosage of LA		
Al Rashoud et al 2014[7]	Saudi Arabia	LA + SLRE + Supportive Education/Advice for KOA	9 sessions over 3 weeks	Placebo-LA + SLRE + Supportive Education/Advice for KOA	6 weeks and 6 months post-treatment
Helianthi et al 2016[8]	Indonesia	LA	2 sessions per week for 5 weeks	Placebo-LA	2 weeks post-treatment
Liao et al 2020[4]	Taiwan (China)	LA	3 sessions per week for 4 weeks	Placebo-LA	No Follow-Ups
Rees 2017[6]	Australia	LA	3 sessions per week for 4 weeks	Placebo-LA	4 weeks and 8 weeks post-treatment
Mu et al 2019[5]	Mainland China	LA + IMS Training	3 sessions per day for 4 weeks	IMS Training	No Follow-Ups

Abbreviations: IMS, Isokinetic Muscle Strengthening; KOA, Knee Osteoarthritis; LA, Laser Acupuncture; RCTs, Randomized Controlled Trials; SLRE, Straight Leg Raise Exercise.

management for KOA,[10] achieving an additional mean reduction of 0.84 cm (with a lower confidence interval of 0.56 cm) with LA represents a potentially meaningful incremental benefit. This could constitute an important option for patients who have contraindications, poor tolerance, or an inadequate response to exercise.

Discrepancy Between Predefined and Applied Inclusion Criteria

Zeng et al specify that eligible RCTs should "randomize participants to laser needle versus placebo laser, exercise therapy, or no treatment",[3] implying that the intervention arm comprises LA alone, while the control arm consists solely of placebo laser, exercise therapy, or no treatment. However, two of the five included RCTs do not meet this criterion: their interventions combine LA with supportive education/advice for KOA and/or exercise,[5,7] and in one trial, the control group also incorporates supportive education/advice for KOA[7] (see our Table 1).

Exclusion of Short-Duration Trials Without Justification

Zeng et al stipulate that only RCTs with a treatment duration of ≥4 weeks are eligible for inclusion,[3] leading to the exclusion of two shorter-duration trials.[11,12] Two associated issues arise.

First, the Saudi Arabian trial referenced earlier involves only nine sessions over three weeks,[7] falling short of the four-week threshold, yet it is nonetheless included.

Second, the rationale for excluding RCTs with treatment durations shorter than four weeks is not provided. We speculate that the authors consider shorter duration indicative of an insufficient therapeutic dose. However, dosage depends not only on treatment length but also on session frequency and laser exposure time per session. For instance, while the included Indonesian trial administers ten sessions over five weeks (two sessions per week), with 80 seconds per acupoint,[8] the excluded Turkish trial delivers ten sessions within two weeks (five sessions per week), applying LA for 20 minutes per session.[12] The total exposure in the Turkish trial is therefore comparable to—or even greater than—that of the included Indonesian[8] and Saudi trials.[7]

In the absence of clear justification, the exclusion of studies with <4 weeks of treatment appears questionable, reduces the number of eligible trials, and potentially weakens the reliability of the meta-analytic synthesis.

Pooling of Heterogeneous Trials and Outcomes at Inconsistent Time Points

Two methodological concerns arise in the pooling of effect sizes.

First, Zeng et al combine the Saudi Arabian RCT (*Intervention*: LA + Exercise + Education/Advice for KOA; *Control*: Placebo-LA + Exercise + Education/Advice for KOA)[7] with three trials comparing LA versus placebo-LA alone, without subgroup analysis. This approach is methodologically questionable due to fundamental differences in trial designs and objectives.

The Saudi trial evaluates whether LA confers additional benefits to routine KOA management, whereas the other three trials assess LA as a stand-alone alternative therapy and whether its effects are specific or nonspecific. Pooling these clinically heterogeneous trials risks introducing statistical heterogeneity and complicating interpretation.

Second, the synthesis of outcome data from temporally inconsistent time points further introduces significant heterogeneity, as visually evidenced by the forest plots (Zeng et al's Figures 4 and 5). Four of the five included RCTs report end-of-treatment outcomes, whereas the Indonesian trial, which involves 10 sessions over 5 weeks, reports outcomes only after the ninth treatment session and at a 2-week follow-up after treatment cessation.[8] Pooling follow-up data from one trial with immediate post-treatment data from others confounds the treatment effect estimate and challenges the interpretation of the pooled result.

Inadequate Investigation of Heterogeneity and Publication Bias

In their meta-analysis, Zeng et al report substantial heterogeneity (I^2 = 83.95%),[3] a critical consideration for interpretation. With only five RCTs included, identifying sources of heterogeneity through meta-regression or similar models is not feasible; the authors' avoidance of such analyses thus reflects methodological prudence. Nevertheless, leave-one-out sensitivity analyses and limited subgroup analyses (eg, separating trials of LA plus routine care from LA alone) remain both viable and informative. While statistical power is limited, their value lies in generating hypotheses regarding potential sources of heterogeneity. Supplementing these with descriptive comparisons of study characteristics and an L'Abbé plot[13] can further strengthen interpretation.

Publication bias is also not assessed. With only five studies, the Doi plot and Luis Furuya-Kanamori Index[14] offer viable alternatives to conventional funnel plots for evaluating potential bias.

Lastly, the authors' assertion that "all studies show that the pain scores in the laser acupuncture treatment group are notably lower compared to the control group, and this high heterogeneity does not compromise the validity of the results" appears overly definitive. Although the direction of effect consistently favors LA or LA combined with routine care, the considerable variation in effect magnitudes (95% CI −1.09 cm to −3.57 cm) is itself notable. This suggests inconsistent treatment responses and implies that the efficacy of LA may be moderated by additional, unexamined factors. Accordingly, the range of effect sizes should be acknowledged as reflecting uncertainty in the magnitude of benefit, rather than asserting uniform effectiveness.

Uncertainty in Adverse Event Evidence and Safety Assessment

Zeng et al report adverse event data from a single RCT (n = 59),[8] yielding a relative risk (*RR*) of 3.52 (95% CI 0.76 to 6.29), which constitutes very low-certainty evidence due to imprecision. The claim that LA has "fewer adverse reactions" than placebo is unsupported, as the *RR* suggests a potential increased risk, and the wide confidence interval reflects inconclusive results. The absence of adverse event data from the other four RCTs, along with insufficient details regarding event types or severity, limits the ability of the SR/MA to evaluate the safety profile of LA—a critical determinant of its application in KOA. Future trials should prioritize standardized adverse event reporting, such as using the Common Terminology Criteria for Adverse Events (CTCAE),[15] to better characterize the safety of LA.

Conclusion and Recommendations

In summary, while Zeng et al's SR/MA provides valuable reference regarding LA for pain management in KOA, its methodological limitations need to be addressed to yield more robust and clinically translatable results. Future research should focus on meticulous data verification and clearer exploration of heterogeneity, objectively and separately evaluating LA as an alternative therapy and as an adjunct to conventional KOA management, to provide more reliable guidance to inform clinical decision-making.

Abbreviations

CTCAE, Common Terminology Criteria for Adverse Events; KOA, Knee Osteoarthritis; LA, Laser Acupuncture; MID, Minimally Important Difference; RCT(s), Randomized Controlled Trials; RR, Relative Risk; SR/MA, Systematic Review and Meta-Analysis.

Author Contributions

Fei-Yi Zhao: Conceptualization, Investigation, Formal analysis, Writing – original draft. Qiang-Qiang Fu: Formal analysis, Validation, Writing – review and editing; Yuen-Shan Ho: Conceptualization, Methodology, Formal analysis, Writing – review and editing.

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