Supportive Care in Cancer (2019) 27:1–2
https://doi.org/10.1007/s00520-018-4345-4

LETTER TO THE EDITOR

Acupuncture for cancer-related fatigue in lung cancer patients: methodological and statistical issues

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Received: 10 January 2018 / Accepted: 6 July 2018 / Published online: 13 July 2018

Dear Editor-in-Chief:

We read with great interest the paper written by Chien-shan Cheng et al. entitled "Acupuncture for cancer-related fatigue in lung cancer patients: a randomized, double blind, placebo-controlled pilot trial," which was published in *Support Care Cancer* in 2017 [1]. The authors aimed to conduct a preliminary evaluation of whether acupuncture is an effective treatment the management of cancer-related fatigue (CRF) by longitudinally measuring symptom improvement and subjective well-being. Chin-shan Cheng and colleagues concluded that the statistical results and clinical observations of their study provided evidence that acupuncture treatment was beneficial for lung cancer patients with CRF. We propose that there are inaccuracies and methodological issues present in the study and that the analysis performed does not justify the considerable effort expended by both the researchers and the participants in the study. The authors have failed to correctly evaluate the differences in the baseline clinical and demographic characteristics between the two studied groups; the patient age and length of treatment as well as the Chinese version of the Brief Fatigue Inventory (BFI-C) and the Functional Assessment of Cancer Therapy-Lung Cancer Subscale (FACT-LCS) scores differ between the studied groups.

First, Chin-shan Cheng et al. indicate that a sample size of 28 was determined to be sufficient to provide evidence of significant differences between the two groups. Such a sample size anticipates an effect size (Cohen's d) of approximately 1.1 (with $\alpha = 0.05$ and $\beta = 0.80$), which, in fact, indicates that the authors were expecting to find a very significant (in clinical terms) effect of acupuncture on CRF treatment. The preliminary data cited by the authors do not support such an assumption and cannot be used for comparison, as the authors do not define how the sample size was determined within the paper.

Second, and more disturbingly, the authors indicate that there were no statistically significant differences in the baseline clinical and demographic characteristics between the two groups included in the study. However, the mean age of the acupuncture group was 58 (5.2) years, and the mean age of the control group (sham acupuncture) was 62 (4.3), which, in fact, represents a statistically significant difference ($P = 0.0358$ or $P = 0.0354$ depending on if there were unequal or equal variances between the groups). Therefore, at the baseline, the mean age between the groups was different. Additionally, the lengths of chemotherapy and radiotherapy treatments in weeks were also different (5.8 (1.2) vs 4.8 (0.8) for the acupuncture and control groups, respectively, which implies $P = 0.0166$ or 0.0154, depending again on if there were unequal or equal variances between the groups).

Third, at the baseline, the two outcomes measured longitudinally in this study were also different between the groups. In this case, the authors report the P values corresponding to the Student t tests; however, we think that such values, as well as the reported mean difference (95% CI), have not been correctly computed. At the baseline (week 0), for the BFI-C, the figures were 6.2 (0.2) for the acupuncture group and 6.6 (0.4) for the control group. The authors reported a mean difference of 0.4 (− 0.5/1.4) and a P value of 0.35 for such a comparison between the groups. We think that a more accurate calculation of the P value for such a comparison is $P = 0.0036$ or $P = 0.0024$, depending on if there were unequal or equal variances between the groups, with a corresponding mean difference of 0.4 (0.1489/0.6511) or 0.4 (0.1544/0.6456), respectively. Similarly, for the FACT-LCS, the authors report 86.4 (2.4) for the acupuncture group and 82.1 (2.5) for the control group, with a mean difference of − 4.2

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(− 11.2/2.8) and a reported value of 0.23 for the between-group analysis. The recalculated *P* values for such a comparison between groups, depending on if there were unequal or equal variances between groups, are both $P < 0.0001$, with a corresponding mean difference of − 4.3 (− 6.2075/− 2.3925) for both conditions. Again, concerning the FACT-LCS, for week 2, the authors report a *P* value for the between-group comparison of 0.11; however, the reported data, in fact, reveal a statistically significant difference between acupuncture and sham acupuncture (recalculated *P* value < 0.001).

Additionally, although the statistical issues are serious enough to merit reanalysis of the discussion and the conclusions of the Chin-shan Cheng et al. paper, there are several methodological issues. The authors indicate that their design is a double-blind trial; however, the same acupuncturist performed the treatment for both groups. Although the researchers were not aware of the treatment allocation, the proposed design may be biased due to the acupuncturist's intervention. Furthermore, the design is not double blind, but rather single blind.

In conclusion, in this study, there were differences between the groups at the baseline in patient age and treatment length. Additionally, at the baseline, there were differences between the two group outcomes measured by the authors, and we doubt that the proposed research design aligns with that of a double-blind clinical trial.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Reference

1. Cheng C, Chen L, Ning Z, Zhang CY, Chen H, Chen Z, Zhu XY, Xie J (2017) Acupuncture for cancer-related fatigue in lung cancer patients: a randomized, double blind, placebo-controlled pilot trial. Support Care Cancer 25:3807–3814. https://doi.org/10.1007/s00520-017-3812-7gej