Author's response to reviews

Title: Feeding, stooling and sleeping patterns in infants with colic - a randomized controlled trial of minimal acupuncture

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Author's response to reviews: see over
Dear Miss Iratxe Puebla, The BioMed Central Editorial Team!

Hereby we re-resubmit the enclosed research paper “Feeding, stooling and sleeping patterns in infants with colic – description of patterns and the influence of minimal acupuncture in a randomized controlled trial”, for consideration for publication in BMC Complementary and Alternative Medicine. The new title is “Feeding, stooling and sleeping patterns in infants with colic - a randomized controlled trial of minimal acupuncture”.

The reviewer’s comments have been addressed and the language has been revised. Changes are marked in red. A point-by-point response (in red) of the reviewer’s comments (in black) follow below.

Reviewer 1:
Discretionary revisions of use of English could be undertaken by authors.
The script has been revised. Changes are marked in red.

Reviewer 2:
Major Compulsory Revisions
1. (Abstract) The study is reasonably well described. However, I believe it is standard, in a clinical trial report, to describe whether the two treatment arms differed with respect to the primary outcome (stooling, correct?). I would therefore ask that this comparison be included in the Results section, before you report the within-group p-values as you do now.
This comparison has been included and the result section now reads:

Results: At baseline when the mean age was five weeks, infants in both groups were fed a median of eight times/day, 148 min/day, with considerable variations. No differences were found between groups in the frequency and duration of feeding during the intervention weeks. Furthermore there were no significant differences between the groups regarding the frequency of stooling, neither at baseline, at which point the infants of both groups had bowel movements 4.2 times/day, nor during the intervention weeks. There was an expected decrease in frequency of stooling in both groups, reaching 2.1 (p=0.001) in the acupuncture group and 3.1 (p<0.001) in the control group. The groups differed regarding large bowel movements
which decreased linearly in the control group (p=0.011) but not in the acupuncture group (p=0.787). More parents in the acupuncture group than in the control group (28% and 15% respectively, p=0.006) experienced the infant’s sleep to be “better” or “much better.” No other significant differences were found. However, parents described a normalized stooling and experienced an improvement in colic in their infants more frequently in the acupuncture group than in the control group.

2. (Statistical and quantitative analyses) I believe you are correctly using nonparametric tests for the analyses, but I am frankly unclear about when the various different tests (Mann-Whitney, Friedman, and “mean rank” – the last one should be better defined) are used. Could you specify which comparisons use which tests, either here or perhaps in the appropriate Tables or points in the text?

If you in fact used Friedman’s test for a repeated measures type of analysis, this should be explicitly explained.

We have specified when Mann Whitney U test and Fridman test was used and added information in Table 2. The text now reads:

“As the Kolmogorov-Smirnov test showed non-normal distribution for core variables, the Mann-Whitney U test was used to analyze differences between groups at each time point. Changes within the groups over baseline and the three intervention weeks were analyzed with Friedman test. P-values < 0.05 were considered statistically significant.

3. (Results) Under “Stooling”, I again believe that the primary between-group analysis should be described first, before you discuss the within-group differences. This is now changed.

When reporting the p-values for this comparison, please state explicitly what test was used for the comparison.

We have added information in “Statistical and qualitative analyses” so that it should be clear that Mann-Whitney U test was used for this comparison.

Also, please state explicitly which test was used to derive the p-values showing significant linear within-control-group declines (p=0.011 is reported) in large bowel movements.

Likewise it should now be clear that Friedman test was used here.
Please also do the same when reporting the Table 2 comparison.

In the caption for Table 2 it is now written that Mann-Whitney U test was used.

In the Table 2 analyses, do the analyses for which the p-values are reported (comparing arms at each week of intervention) take each child’s baseline level into account?

As no significant differences between the groups were detected at baseline we did not find it necessary to adjust individual values for baseline values.

Minor essential revisions

1. (Abstract) In conclusions, “out ruled” should be written as “ruled out”.
   This is now changed.

2. (Limitations) “exact measured” should read “exactly” or “precisely” measured.
   This is now changed.

Discretionary revisions

1. (Abstract) I would personally again state in the conclusion that this study was negative, although a minor effect of acupuncture cannot be ruled out.

   We have taken this view into account. The Conclusion section in the Abstract is rewritten and now reads: “Infants with colic in the present study had a higher frequency of stooling than reported internationally in healthy infants. Minimal acupuncture had no major effect on feeding, stooling and sleep, although a minor effect of minimal acupuncture on stooling and sleep cannot be ruled out.”

   The longer Conclusion section at the end of the article now reads: “Minimal acupuncture in the point LI4 twice a week for 3 weeks only showed a minor difference in the frequency of stooling between the groups. The parents in the acupuncture group more frequently commented on a changed and normalized stooling in their infants, and more frequently reported improvement of sleep and colic. As the correlation between relief of colic symptoms and frequency in feeding and stooling is weak there may be other explanations for the effect on crying induced by acupuncture. Further studies are requested to clarify the mechanism of acupuncture in colic.”
2. (Design or statistical analyses) Would you be able to state anything about the expected power of your study (when you were designing it) to detect expected, or clinically important, differences in the outcomes being examined in this report?

As stated in Statistical and qualitative analyses the power calculation was based on assumptions of how acupuncture would affect the primary outcome of crying. No power calculation was performed on how acupuncture would affect feeding, stooling or sleep. We have added a sentence about this in “Strengths and limitations”: “Power calculation was done on the variable crying, reported in an earlier article [19] and not on variables as stooling or feeding which might have resulted in another number of participating infants.”

3. (Overall) I am not a clinician, but I was a bit surprised that you did not include a brief discussion of the other reported results from this study, ref 19, in this current paper. I have not read this other paper in detail, but it showed that acupuncture was helpful in reducing crying and fussing over the first two weeks? What are some reasons this benefit might not have carried over to these secondary outcomes?

We have now considered this and added text at the end of the Result and discussion section and even suggested mechanisms for the acupuncture effect:

“No definite statistical conclusions can be made on independent variables like the parents comments above. However, the parents perception of normalized stooling, better sleep and better progress of the colic are in line with the results reported earlier: the infants in the acupuncture group cried and fussed less and the mean value for crying was below the limit for colic after the first intervention week [19]. The infants in the acupuncture group reached normal levels for their age of the stooling frequency in the third intervention week (Table 2), ie < 2.2 stoolings/day, [7, 9-11]. The largest reduction of both crying and stooling frequency was measured after the first acupuncture treatment. However, the differences in feeding and stooling patterns between the groups are not significant in the majority of the variables and the present study cannot support a simple correlation between reduction of crying and an improved regulation of these. The effect of acupuncture may as well be of different origin such as spasmolytic or sedative.”

In the section Strengths and limitations we added: “Power calculation was done on the variable crying, reported in an earlier article [19]. Another limitation of this article is that no correlation analyses was done to see if the individual crying and stooling patterns were
correlated in each child, and if the experience of normalized stooling or general improvement according to the parent was correlated to reduced crying in the infant.”

Yours sincerely,
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