Science Media Centre Roundup

EMBARGOED UNTIL 23.30 UK TIME on Monday 16 January 2017

Expert reaction to acupuncture to treat colic as published in *Acupuncture in Medicine**

Prof David Colquhoun FRS, Professor of Pharmacology at University College London, said:

"It is truly astonishing that, in the 21st century, the BMJ still publishes a journal devoted to a form of pre-scientific medicine which after more than 3000 trials has still not been able to produce convincing evidence of efficacy[1]. Like most forms of alternative medicine, acupuncture has been advocated for a vast range of problems, and there is little evidence that it works for any of them. Colic has not been prominent in these claims. What parent would think that sticking needles into their baby would stop it crying? The idea sounds bizarre. It is. This paper certainly doesn't show that it works.

"The statistical analysis in the paper is incompetent. This should have been detected by the referees, but wasn't. For a start, the opening statement, 'A two-sided P value ≤0.05 was considered statistically significant' is simply unacceptable in the light of all recent work about reproducibility. Still worse, Table 1 uses the description 'statistical tendency towards significance (p=0.051–0.1)'.

"Worst of all, Table 1 reports 24 different P values, of which three are (just) below 0.05. Yet no correction has been used for multiple comparisons. This is very bad practice. It's highly unlikely that, if the proper correction had been done, any of the results would have given a type 1 error rate below 5%.

"Even were it not for this, most of the 'significant' P values are marginal (only slightly less than 0.05). It is now well known that the type 1 error rate gives an optimistic view. What matters is the false positive rate - the chance that a 'significant' result is a false positive. A P value close to 0.05 implies that there is at least a 30% chance that they are false positives. If one thought, *a priori*, that the chance of colic being cured by sticking needles into a baby was less than 50%, the false positive rate could easily be greater than 80%[2]. It is now recognised that this misinterpretation of P values is a major contributor to the crisis of reproducibility.

“Other problems concern the power calculation. *A priori* calculations of power are well-known to be overoptimistic, because small trials usually overestimate the effect size. In this case the initial estimated sample size was not attained, and a rather mysterious recalculation of power was used.

“Another small problem: the discussion points out that ‘the majority of infants in this cohort did not have colic’.

“The nature of the control group is not very clear. An appropriate control might have been to cuddle the baby - this was used in a study in which another implausible treatment, chiropractic, was shown not to work[3]. This appears not to have been done.

“Lastly, P values are reported in the text without mention of effect sizes. This is contrary to all statistical advice.

“In conclusion, the design of the trial is reasonable (apart from the control group) but the statistical analysis is appalling. It's very likely that there aren't any real effects of acupuncture at all. This paper serves more to muddy the waters than to add useful information. It's a model for the sort of mistakes that have led to the crisis in reproducibility. The BMJ should not be publishing this sort of stuff, and the referees seem to have no understanding of statistics.”

[1] Colquhoun & Novella. 2013. *Anesthesia & Analgesia*, 116, 1360 - 1363 (reprint)

[2] http://rsos.royalsocietypublishing.org/content/1/3/140216

[3] Olafsdottir et al 2001, reprint

Prof George Lewith, Professor of Health Research at the University of Southampton, said:

“This looks to me to be a good sized fastidious well conducted study (Cochrane A for an acupuncture trail in which the therapist cannot be blinded). The outcome is clear and the power of the study seems reasonable which suggests that MA is a reasonable and as far as we know safe intervention for infantile colic. Three out of 4 similar studies come to this conclusion so a systematic review would be a good idea and even better an individual patient data (IPD) meta-analysis. The evidence of acupuncture’s safety is conclusively established in adult medicine so suggesting this intervention is safe is reasonable in spite of the limited safety data in children. It’s too small a study to be conclusive on its own but as there is no proven conventional

treatment for infantile colic one could argue there is more evidence for acupuncture than conventional best practice."

Prof Edzard Ernst, Emeritus Professor of Complementary Medicine at the University of Exeter, said:

"This study shows almost the opposite of what the authors conclude. Both minimal and traditional Chinese acupuncture seemed to reduce the symptoms of colic compared to no acupuncture at all. This confirms previous research showing that acupuncture is a 'theatrical placebo'.

"The study was designed without an adequate placebo group; therefore, conclusions about specific therapeutic effects of acupuncture are not permissible.

"We know that colicky babies respond even to minimal attention, and this trial confirms that a little additional TLC will generate an effect. The observed outcome is therefore not necessarily related to acupuncture."

Before The Headlines

COMMENTARY
Title, Date of Publication & Journal
Effect of minimal acupuncture for infantile colic: a multicentre, three-armed, single-blind, randomised controlled trial (ACU-COL) Landgren K, Hallström I. *Acupuncture in Medicine* 2017;0:1–9.
Study's main claims – and are they supported by the data
The paper does not support the claim that acupuncture cures or alleviates colic in babies. The paper lends very weak support to the claim that minimal acupuncture (a specific type of acupuncture) *could* provide some benefit for colicky infants. But given the lack of any known biological mechanism that could explain how this effect could work, a stronger statement than that is not plausible. The methodology for the study is fairly rigorous and the investigators have clearly taken steps to ensure that bias is minimised. However there are concerns regarding

how well blinding was maintained in practice, the large number of analyses performed (only a few of which were significant) and the potential bias incurred by combining the two acupuncture groups post hoc. There is also an imbalance between the two groups in terms of the percentage of mothers breast-feeding, which doesn't appear to have been accounted for in the analysis or discussion.

Strengths/Limitations

The researchers have clearly taken blinding very seriously in this study and have painstakingly documented the steps they took to ensure that parents and nurses did not know beforehand which treatment group the infant had been assigned to. However, Table 5 clearly shows that more parents of infants receiving acupuncture believed that that's what they were receiving compared to the percentage of parents in the control group who believed they were receiving acupuncture. (If blinding had been completely maintained, we would expect these numbers to be roughly equal.) The authors casually suppose that this was because the parents were observing a benefit of acupuncture but it seems just as likely to be due to other factors such as marks on the skin or drops of blood where the needles had been.

There was a (presumably random) imbalance in breastfeeding between the acupuncture group (62%) and the control group (49%) (Table 1). As the first paragraph implies that diet is an important risk factor for colic it is surprising that this imbalance is not discussed more in the paper or controlled for in the analysis.

At some point during the trial, it was decided that the two acupuncture groups should be combined in the analysis due to external factors (acupuncture becoming available as a matter of routine whilst the trial was ongoing). It is not clear whether this decision was made whilst still blind to the data that had already been collected or not. It is possible that having a look at the data beforehand could have influenced the decision of whether or not to change the planned analyses mid-stream.

It should also be noted that there are a large number of comparisons being performed, increasing the likelihood of a spuriously significant result being observed by chance. The p-values (mostly in the 0.03 to 0.05 range) do not indicate an overwhelmingly strong signal, and as such I suspect that these would cease to be significant if appropriate adjustments for multiple comparisons were made.

Glossary

n/a

Any specific expertise relevant to studied paper (beyond statistical)?

None

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* 'Effect of minimal acupuncture for infantile colic: a multicentre, three-armed, single-blind, randomised controlled trial' by Kajsa Landgren and Inger Hallström will be published in *Acupuncture in Medicine* at 23.30 UK time on Monday 16th January, which is also when the embargo will lift.

Declared interests

Prof Ernst: I have no conflicts of interest. I have been an acupuncture researcher for over 25 years; I have published over 100 papers on the subject.

Prof Colquhoun: No conflicts of interest.

Note to editors

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The SMC has asked the experts in the above Roundup to declare any interests which may be regarded by a reasonable and objective third party as giving rise to a conflict, and their responses are included above.

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