Author's response to reviews

Title: A double blind, randomised placebo controlled trial of topical 2% viscous lidocaine in improving oral intake in children with painful infectious mouth conditions.

Authors:

Sandy M Hopper (sandy.hopper@rch.org.au)
Franz E Babl (franz.babl@rch.org.au)
Michelle McCarthy (mccarthy@rch.org.au)
Chasari Tancharoen (c.tancharoen@ugrad.unimelb.edu.au)
Katherine J Lee (katherine.lee@mcri.edu.au)
Ed Oakley (ed.oakley@southernhealth.org.au)

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Author's response to reviews: see over
Rachel Neilan
Executive Editor
BMC-series Journals
BioMed Central Floor 6,
236 Gray’s Inn Rd
London, WC1X 8HL

14 October 2011

Your Ref: MS: 4308180945462727

Dr Neilan

Please find the revised BMC Pediatrics article entitled:

**A double blind, randomised placebo controlled trial of topical 2% viscous lidocaine in improving oral intake in children with painful infectious mouth conditions.**

We have revised the manuscript in response to your suggestions in email dated 1 October 2011.
In short, all suggestions have been incorporated into the manuscript and the attached table details our responses.
Please do not hesitate to contact me with any questions.

Yours sincerely

Ed Oakley
Director Paediatric Emergency Medicine, Southern Health Chair Paediatric Research in Emergency Departments International Collaborative (PREDICT)
e: ed.oakley@southernhealth.org.au
p: +61 3 95942707
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<tr>
<th>Issue Number</th>
<th>Editor's comment</th>
<th>response</th>
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<tbody>
<tr>
<td>1.</td>
<td>From the methodical point of view, is it correct to include the 20 pilot children into the final analyses?</td>
<td>We argue that it is correct to include the pilot data as: This was part of the original study design (a form of adaptive trial design). The interim analysis was pre-planned solely to inform the power calculation for this study, as there are no prior data on the endpoint from which to carry out a sample size calculation. The analysis for the interim report was restricted to the primary outcome data only. All study procedures remained unchanged after the interim analysis. Blinding of individual patients was been maintained during the interim analysis with only the statistician who prepared the report seeing the unblinded patient data.</td>
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<td>2.</td>
<td>The age distribution of the subjects is quite large. It may happen that a randomisation without stratification may make the groups as very different. Is there any reason to believe that age could be a (strong?) confounder? If not, my opinion is that the study design is acceptable.</td>
<td>The majority of patients in both groups will be younger than 4 years old, although there will be some children older than 4 years (based on our inclusion criteria 6 months to 18 years). It is possible children older age than 4 years respond differently towards the drug and in particular in terms of the amount of fluid they drink, and as pointed out there may be a chance imbalance in the number of older children in the two intervention groups, which could confound the treatment effect. As the trial is underway, it is not possible to stratify the randomisation at this late stage. However we will amend the protocol to specify that we will carry out a sensitivity analysis where we calculated the treatment effect adjusted for age in case there is a chance imbalance. See the manuscript: (METHODS/DESIGN section; Subsection: “Sample size, power and statistical methods”; page 9, paragraph 3) ADDITION OF TEXT: “As a sensitivity analysis, all treatment comparisons for primary and secondary outcomes will also be presented adjusted for age at presentation to account for any chance imbalance between the treatment groups with respect to this potentially confounding factor using linear and logistic regression models for continuous and binary outcomes respectively.”</td>
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<td>3.</td>
<td>In addition, please include your trial registration number at the foot of your abstract on the submission system.</td>
<td>This has been done. “This study is registered with the Australian New Zealand Clinical Trials Registry, 9 July 2009, ACTRN12609000566235”</td>
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