Reviewer's report

Title: How effective is Ametop 4% gel, before a peripherally inserted central catheter, in reducing procedural pain in infants: a randomized double-blind placebo controlled trial [ISRCTN75884221]

Version: 2 Date: 5 January 2006

Reviewer: Anna Taddio

Reviewer's report:

General
RCT of Ametop vs Placebo for PICC insertion. It is of interest to clinicians and scientists in the field. / Recommend using generic drug name throughout manuscript.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Abstract appears to be missing and one is needed.
2. Pg 3 - More information on rationale for study is needed in light of fact that similar study previously published by Ballantyne et al.
3. Pg 5, 1st para: indicate who obtained consent.
4. Pg 5, 2nd para: Indicate here that drug was administered under occlusion. Was the dose 1.1g?
5. Pg 5, 3rd para: what is stability of drug when removed from original package? It is our experience that the drug crystallizes after days to weeks and according to manufacturer, is not effective at this point. This is a critical issue.
6. Pg 7, 1st para: After reading the entire manuscript and seeing that no infant received sucrose, I see no reason to mention it-delete.
7. Pg 7, 2nd para: Remove Table 1 and summarize information in manuscript.
8. Pg 8, 2nd para: How was PIPP scored-give details. Who recoded tapes, how many tapes? What is the statistic used for inter- and intra-rater reliability? Was it done at Dr. Stevens' lab at SickKids?
9. Pg 9, 2nd para: PIPP at first minute cited as secondary outcome here (and primary outcome in previous paragraph-please correct). Is insertion phase same as skin puncture phase-be consistent. Who measured ease of insertion?
10. Pg 9, 3rd para: Why were the tests specified used to assess safety? Cite literature demonstrating that drug may affect these parameters. Was extra blood/procedures done for the purposes of this study?
11. Pg 10, 1st para: cite Ballantyne paper.
12. Pg 11, 1st para: PIPP contains GA so why is it adjusted?
13. Pg 12, 2nd para: Remove sucrose. The PIPP scores are lower for drug-this should be mentioned. Specify "mean oxygen saturation" in last line. I would prefer to see these physiologic responses, for poke and baseline (or difference scores).
14. Pg 13, 2nd para: First paragraph of discussion weak-specific findings of the study. A power calculation appears to be in order.
15. Pg 14, 3rd para: This doesn't appear to be relevant-delete.
16. Pg 16, 1st para: Similar analysis by Ballantyne-belongs in results section, not here. Remove Figure 2-does not add any value.
17. Pg 16, 3rd para: Sucrose not evaluated in this trial-may write about its potential role. Why not discuss opioids also?
18. Pg 17, 2nd para: Number of painful interventions likely to be balanced between groups. I don't see this as a major limitation.
- Include information on why outcomes not available for all infants.
- Important to talk about how outcomes were different between this study and Ballantyne. Also, the lower limit of effectiveness of the drug is 30 minutes, and longer application times are needed for optimum effect. This study used 30 minutes and this is a limitation that should be acknowledged. Did the investigators wait exactly 30 minutes before removing the gel? What was the elapsed time between drug removal and procedure?

19. Pg 17, 2nd and 3rd para: conflicting information about using systemic analgesia vs. sucrose? What do authors recommend? Why was their study negative? Do they think local anesthesia offers any benefit at all?

20. Table 4: For number of attempts, is difference between 2 and 1 really 0?

21. Figure 1: Can show number qualifying for secondary outcomes.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

The manufacturer of Ametop funded an immunization study to the reviewer within the past 5 years.