Author's response to reviews

Title: Single application of 4% dimeticone liquid gel versus two applications of 1% permethrin creme rinse for treatment of head louse infestation: a randomised controlled trial.

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Dear Editors

First I would like to thank my three reviewing colleagues for their very helpful suggestions and comments. I have made revisions to the manuscript in line with those comments as follows:

Review by Rémy Durand

2. The last two sentences starting from “In those who did have lice...” have now been moved into the Discussion section and the order of words changed to suit that position.
3. As suggested I have entered an estimated cost figure per individual for both treatments. However, I was not sure which currency unit to use so I have selected the Euro, mainly because Hedrin Once is available widely in the European Union but not in North America. Please advise if you would prefer another currency.
4. I have restructured part of the Discussion section dealing with use of permethrin to explain why the material was selected (widespread use, familiarity with regulatory authorities) and why malathion was not selected (diversity of formulations making them not comparable and non-availability of the only product still listed in the UK).

Review by Ariel Toloza

The comment/question by Dr Toloza is not easy to answer within the manuscript. For estimation of sample size a reasonable balance need to be retained between minimising exposure of participants to investigative procedures and obtaining adequate data to fulfil the purpose of a study. In this case the estimation was based on a “potential” efficacy for the permethrin comparator that, although optimistic, was not outside the bounds of possibility, in a similar manner to the
way the estimation of efficacy for the dimeticone preparation was based on what
the sponsor would have anticipated should all aspects of the study proceeded as
they may have hoped. The other aspect of the balance is to obtain an estimate of
numbers that is consistent not only with demonstrating the level of difference
between treatments but also demonstrating the safety of the treatment regimen
in use. This necessarily requires adequate numbers per group to satisfy the
perceptions of the statistician advisors to both the ethics committee and the
competent authority (MHRA). Given the sponsor estimate of how well they
expected their product to perform (around 90% success) and the realistic view of
how permethrin might fail to perform (15-20% success) and using standard
approaches to confidence (95%) and power (80%) the numbers per group would
have been 8 participants, clearly so open to statistical noise that almost any
result would have been meaningless. Even increasing the both levels of
confidence and power to 99% the numbers per group would only have increased
to 18 participants. Had we had prior knowledge of the outcome and used a true
estimate, i.e. 70% success for dimeticone and 15% for permethrin, with 95%
confidence and 80% power, the numbers would have only been 15 per group
increasing to 36 per group for 99% confidence and 99% power. Thus, in
satisfying the anticipated estimated bottom end number acceptable to the
statisticians involved (of 40 based on previous experience) this somewhat
artificial estimate was derived, which would address all possible eventualities of
unprecedented outcomes, including drop out and unexpectedly high rate of
failure for the dimeticone, and provide sufficient data to be confident of a true
outcome that would be acceptable for regulatory purposes in those territories in
which the dimeticone product was seeking regulatory approval.

Review by John Clark

1. I have now ensured consistency in the order of placing reported data for the
two treatments as requested.

2. The Odds Ratios have been included for outcomes primarily because the
current trend in presenting comparative data for treatment outcomes in clinical
evidence reviews employs ORs more frequently than other measures (e.g.
Absolute Risk/Rate, Relative Risk/Rate, etc). I can understand Dr Clark’s
question as to the value but the primary justification for including them is that in
the absence of quoting such data it has been a trend in some CE reviews to
“mark down” in quality studies that do not contain them.

3. I can fully understand Dr Clark’s puzzlement over the difference between
“ovicidal activity” and “inhibition of egg hatching”. I apologise for omitting to
qualify these two criteria and I have now added a clarification point after the first
mention of these in the text. Primarily they were the product of a statistical
algorithm to make distinctions between a single treatment regimen and a double
treatment application regimen in that “inhibition of egg hatching” referred to
prevention of eggs hatching/nymphs emerging at any point during the post
treatment assessment period and “ovicidal activity” referred specifically to no
eggs hatching after the completion of treatment. Thus the two criteria are
identical for the single application treatment regimen but, in the case of the two
applications regimen, some eggs hatched during the period between treatments, showing that eggs were not de facto inhibited from hatching by applying the product.

Regards

Ian F Burgess