Author's response to reviews

Title: A multi-centre randomised double-blind placebo-controlled trial to evaluate the value of a single bolus intravenous alfentanil in CT colonography

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Author's response to reviews: see over
Dear dr. Manibo,

Thank you for sending the comments on manuscript 2372811679070196 entitled ‘A multi-centre randomised double-blind placebo-controlled trial to evaluate the value of a single bolus intravenous alfentanil in CT colonography’. We studied the reviewer comments carefully and made adjustments accordingly. We thank the reviewers for their comments that enabled us to make substantial improvements to the manuscript.

Below we give a point-by-point response to all comments. In our manuscript we highlighted all changes using the ‘track changes’ function. In addition we placed text boxes next to the changes containing the reviewer (A.I. and A.S.) and the comment number.

Kind regards,
Also on behalf of the co-authors,

Thierry Boellaard

Responses to reviewer Ana Ignajtovic:

Comment 1
Abstract – results line 3 – requires p values

Response 1
We added p values to line 3 of the abstract results (page 4, line 15).

Comment 2
Methods – population – line 1: Were the pts consecutive?

Response 2
The patients in this study were indeed consecutive. We added the word ‘consecutive’ to the first sentence of the population description of the method section. (page 7, line 23)

Comment 3
Methods – intervention – there are no comments about allocation concealment mechanisms – please amend. Who recruited the pts and who assigned the treatment – please clarify

Response 3
We added several sentences to clarify our allocation concealment mechanism and our recruitment procedure and our assignment procedure:
‘Patients were assessed for eligibility by telephone by one of the research physicians (T.N.B., M.P.P. or L.J.S.).’ (page 8, line 1-2)

Two research physicians (J.H.R and M.C.H.) generated a randomisation list using nQuery. The list was kept by three research physicians (J.H.R, M.C.H. and J.A.W.T.) not involved in the patient recruitment, CT colonography procedure or data collection. (page 8, line 19-21)

‘Study medication was prepared by the physicians who kept the randomisation list. The medication ampule was placed in a signed sealed envelope near the CT scanner room to allow deblinding in case of a medical emergency.’ (page 8, line 25 until page 9, line 2)

‘After the procedure one of the physicians who kept the randomisation list collected the envelope.’ (page 9, line 4-5)

Comment 4
Outcome measures – should come earlier in the paper – only primary outcomes stated- please clarify if the secondary outcomes were set at the beginning of the study – this refers again to Conclusion line 4 – all the other outcomes are at present hypothesis generating (reduced procedural time, recovery time and safety) as study not powered to assess – please clarify.

Response 4
We changed the position of the outcome measure to page 7, line 12-16. We added the secondary outcomes that we had defined before the study:
Secondary outcome measures were differences between patients receiving alfentanil and placebo regarding: pain scores per insufflation position, pain and burden of the CT colonography procedure and individual CT colonography aspects (e.g. insufflation, bowel preparation etc.), side effects, vital parameters, procedure time and recovery time. (page 7, line 17-20)

We added to our conclusion:
‘Our secondary outcomes such as the total procedural pain and burden, the effect on procedure time and recovery time should be confirmed in for these outcomes appropriately powered studies.’ (page 18, line 11-14)
Comment 5
Table 1 – please insert total numbers as well as percentages

Response 5
We added the total number in Table 1 for all percentages (page 27). We also added a sentence to the table legends to explain this: For all percentage the numbers are given between brackets. (page 27, line 4-5)

Comment 6
It is of great significance that 16/36 pts experienced episodes of desaturation – please elaborate in the conclusion in terms of safety

Response 6
We do understand your concerns about the large percentage of patients with desaturations very well. However all desaturations were short lasting, self limiting and no interventions were needed. Therefore our anaesthesiologists do not deem the desaturations we observed in our study of great significance.

We added a sentence in the conclusion to specify this:
‘Although desaturations were frequently observed with alfentanil, these were not considered clinically relevant because they were all short lasting and self limiting’ (page 18, line 5-7)

Responses to reviewer Andrew Slater:

Comment 1
Reference 18, 'JAMA' in capitals

Response 1
Reference 18: We changed ‘jama’ into ‘JAMA’ (page 21, line 18)

Comment 2
Reference 24 doesn't make sense

Response 2
Comment 3
Discussion: 'Pain was assessed in prone position only'. According to table 2 pain was assessed in all 4 positions

Response 3
We understand the confusion. Before acquiring scan acquisitions we insufflated in three positions: right lateral decubitus, supine and left lateral decubitus. Thereafter we made scan acquisitions in prone and supine position. We asked for numeric pain rating during all insufflation positions before scanning. Additionally we asked in the prone scan acquisition position, but not in the supine scan acquisition position.

We added to the legends of Table 2: ‘Pain scores 1, 2 and 3 were asked before performing the scan acquisitions. Pain score 4 was asked with the patient in the prone scan position. No pain score was asked during the supine scan position.’ (page 28, line 4-7)