Author's response to reviews

Title: Selective decontamination of gastrointestinal tract in patients with oesophageal resection

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Version: 4 Date: 24 August 2010

Author's response to reviews: see over
To Editorial Team

Object : 1482889314370974 - Selective decontamination of gastrointestinal tract in patients with oesophageal resection

We thank you and the reviewers for your helpful comments and are grateful to re-submit our manuscript “Selective decontamination of gastrointestinal tract in patients with oesophageal resection“. The following changes were made according to the reviewers comments (including changing to the journal style):

Reviewer's report

Title: Selective decontamination of gastrointestinal tract in patients with oesophageal resection

Version: 2 Date: 4 June 2010

Reviewer: Johan I van der Spoel

Reviewer's report:

Major:
- The authors need to explain why - in contrast to the "full SDD regimen" - apparently no oral component of SDD (the oral paste, Orabase) is used and why not a 3-4 days course of cefotaxim was used but only one dosis (in longer operations 2 doses) of cefamandol. They also need to explain why nystatine was used instead of amfotericineB.

- The solution of polymyxin, tobramycin, vancomycin and nystatin was given orally (see page 7, second paragraph). However, no oral additional paste was used according to the regimen proposed by Schardey et al.

- As a perioperative antibiotic prophylaxis one dose of cefamandol was used following the hospital guideline.

- Nystatine was used instead of amphotericin B because of an internal regulation of the hospital pharmacy. Amphotericin B is no longer delivered.
- Were surveillance cultures taken? What were the pathogenic microorganisms in the SDD-patients with pneumonia and leakage? Were they susceptible to the SDD-components, and if yes: please comment on the apparent failure of SDD

- No, there were no cultures taken. Because of the retrospective data, no data concerning pathogenic microorganisms is available.

Minor:
- Please explain in the text where the abbreviation PTY stands for; why not use "SDD"?

- We changed “PTV” in “SDD” throughout the manuscript

Discretionary
- Almost all the result section could be put into tables for more ease reading

- Done

-Would it be possible to elaborate on a difference in Length of Stay (in the ICU) between SDD and non-SDD patients?

- No difference in the length of stay in the ICU was found. Differences in the length of stay in the hospital are mentioned on page 10.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests. JI van der Spoel

Reviewer's report

Title: Selective decontamination of gastrointestinal tract in patients with oesophageal resection

Version: 2 Date: 20 July 2010

Reviewer: Anne De Smet

Reviewer's report:

Major Compulsory Revisions
Abstract
1. Page 2, Results: Compared to a retrospective cohort group, patients with PTV
had significantly less….etcetc. The first part of this sentence has to be added to prevent misinterpretation

- Done

2. Page 3, Conclusions: ………in patients with distal oesophageal anastomosis compared to an historical control group. See comment before.

- Done

Methods
3. Page 8, second paragraph: was the intravenous ab prophylaxis with identical to the treatment in the retrospective cohorts (with or without PTV/SDD)?

- Yes, the intravenous perioperative antibiotic was identical in the retrospective and in the prospective group following the hospital guidelines. This is also why cefamandol was used.

4. Page 8, last paragraph: when did the historical cohort group start? From ?? until 2002. Is it possible that in the earlier years relatively less patients received PTV/SDD? If so, there is a possible imbalance between the historical cohort groups with a control group (historical cohort without PTV/SDD) with more patients treated in earlier years than in later years. (prospective cohort—retrospective cohort with predominantly PTV/SDD—older retrospective cohort predominantly without PTV/SDD). As the authors state themselves in the discussion: the development of ICU treatment (and surgical techniques) might have influenced the results. It is essential that the authors clarify for the historical cohorts how many patients were treated every year with or without SDD/PTV, this can be added to figure 1.

- The historical cohort started in 1995. We changed it to “from 1995 until 2002”.
- Yes, in the earlier years less patients were treated with SDD. Actually from 1995 until June 1998 no patients received SDD. In July 1998 SDD was started. The historic group without SDD was treated before the introduction of SDD at our hospital in 1998.
- It is added to figure 1.

Discussion
5. Page 13: In the beginning of the discussion the authors should state in the conclusion that all is in comparison to an historical control group. The conclusion should be more careful, this is solely a hypothesis generating observational study.

- We thank you for this important comment. “This observational study generates the hypothesis SDD in patients receiving a distal oesophageal anastomosis have reduced perioperative morbidity and mortality.” Was added to the discussion section.

Minor Essential Revisions
Abstract
6. Page 2, Background: Please explain what is meant by PTV (used as abbreviation throughout the manuscript), usually Selective Decontamination of the Digestive Tract is abbreviated as SDD, consider changing PTV in SDD

- We changed “PTV” in “SDD” throughout the manuscript

Background
7. Page 4, Line 6: Please explain more about the concept of SDD since this is not known to every reader and it consists of more than just elimination of Gram-negative bacteria. This will also clarify the choice of combination of antibiotics in the SDD/PTV. (For instance: It consists of prevention of secondary colonization with Gram-negative bacteria, S. aureus and yeasts through application of non-absorbable antimicrobial agents in the oropharynx and gastrointestinal tract, and maintaining the anaerobic intestinal flora through selectively using antibiotics (both topically and systemically) without anti-anaerobic activity.

In the ICU it is usually accompanied by pre-emptive treatment of possible infections with commensal respiratory tract bacteria through systemic administration of cefalosporins during the first four days in ICU

- We added “By topical application of nonresorbable antimicrobial agents in the oropharynx and gastrointestinal tract, the secondary colonization with Gram-negative bacteria, S. aureus and yeasts should be prevented. To maintain the anaerobic intestinal flora only selective antibiotics (both topically and systemically) without anti-anaerobic activity were used. The aim of these measures is to reduce the incidence of perioperative nosocomial infections.”

8. Page 5, fifth line from below: to hypothesise a lower etc is difficult to understand.
I would suggest: Consequently all patients undergoing a total or partial oesophagectomy etc etc...and prospectively recorded to determine the perioperative morbidity and mortality (especially......) compared to a retrospective control group

- Done

Methods:
9. Page 7, Line 3: prospectively recorded and retrospectively analysed# Did the authors decide on the endpoints before or after starting the prospective cohort?

- We decided on the endpoints before starting the prospective cohort.

10. Page 7, Line 5-7: The reasons for excluding transmediastinal procedure are mentioned, please explain why patient having subtotal gastrectomy, transthoracic oesophagectomy were excluded? (in contrast what seemed to be the earlier plan: see background section page 5 where it is stated that all these mentioned groups were prospectively recorded) Did the authors consider a (pre-planned) subgroup-analysis?
• Transthoracic oesophagectomy was excluded since according to the hospital policy all these patients have cervical anastomosis and no intrathoracic anastomoses were performed.

• Subtotal gastrectomy was excluded because a gastro-jejunostomy was considered to be a different entity.

• These two explanations are now also mentioned on page 7.

11. Page 7, Line 15: please explain why vancomycin is added, usually it is because of high endemicity levels of MRSA.

• Vancomycin was added to eliminate gram-positive organisms following the concept of Schardey et al.

12. Page 7, Line 14: polymyxin instead of polymycin (and tobramycin instead of tobramyxin on page 2.)

• Done

13. Page 7, Line 18: was this at least 24 hours before operation or less? Did all patients receive 4 dosages of SDD/PTV before operation or less? And was this also the case in the retrospective SDD/PTV group?

• Patients received SDD starting in the morning of the day before surgery and received at least 4 doses before surgery. The regimen was not altered between the prospective and the retrospective group.

• It’s now mentioned in the text (page 7)

14. Page 9, second paragraph medical ethics committee? To me it is not clear what the ethics committee exactly decided upon and whether they were asked or not to decide upon a (double-blind) prospective study. In the discussion (page 14) it is stated that a prospective study would not be approved, but not the reason why. Or is it something the authors suppose and they didn’t try? If the MEC really decided on that, it should be mentioned in the methods.

• On page 9 “The local ethical commission…for Medical Confidentiality” is changed to “The medical ethics committee allowed the analysis of these data” for easier understanding.

• On page 14 the part with the approve of a prospective study is not mentioned any more.

Results
15. Page 10: Retrospective analysis
Retrospective groups with PTV? # looking at the numbers the retrospective group of 53 patients is meant.
In this paragraph it is mentioned that in the retrospective SDD/PTV cohort 2 out
of 53 patients died within the first 30 days, in contrast to 1 out of 53 patients in the longitudinal analysis on page 11. What is the correct number of patients who died in this group?

- “groups” is changed to “group”
- We thank for this important hint: The correct number is 1 out of 53. We corrected it on page 10.

16. A table with all results would be helpful, consider adding Odds Ratios (including 95% CI) (retrospective PTV vs retrospective non PTV, prospective PTV vs retrospective non PTV, prospective PTV vs retrospective PTV)

- Done. We additionally changed in table 1 and 3 two columns

Discussion

- It’s now on page 14. We added “Additionally in one trial in the latest Cochrane review on antibiotic prophylaxis/SDD was no resistance showed. In the study of de Jonge they even noted lowered development of resistance among SDD-treated patients in intensive care over a 27-month period.”
- The two studies are listed on “references” [18 and 19]. The study of Roos et al. is now number 20.

18. Page 15 : last sentence: …to plan a double-blind randomized controlled prospective study….

- Done

19. Table 1:
Length of stay in the hospital is not a baseline characteristic but a potential endpoint/result.

- “length of stay in the hospital” is removed. It’s also removed in the text (second paragraph).

Discretionary Revisions
Background:
20. Page 4, Line 10: by far of so far?

- We changed this to “so far”

21. Page 5, Line 16: Based on this experience (own can be removed)
Methods:
22. Page 7, Line 2: at a tertiary referral hospital

Results:
23. Page 11, last paragraph, last sentence: Patients with PTV developed less often pneumonia postoperatively (4.9% etc), compared to etc

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being Published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests