Author's response to reviews

Title: Risk of Contamination of Nasal Sprays in Otolaryngology Practice

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Author's response to reviews: see over
To: Dr. Jo Appleford  
Senior Assistant Editor  
BMC-Series Journals  

MS: 1011840621111893  

26 December 2006  

Dear Dr. Appleford,  

Paper: Risk of Contamination of Nasal Sprays in Otolaryngologic Practice  
Authors: Erdinc Aydin, Evren Hizal, Babur Akkuzu and Ozlem Azap  

We have revised the above paper in line with the referees’ and editor’s comments. Please find attached a “word.doc” file of the amended version, which we would like to resubmit for publication in BMC- Ear, Nose and Throat Journal. 

A list of changes made in the manuscript and our reply to the referee’s report are given on the following pages.  

Sincerely yours,  

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List of changes made in the manuscript (MS: 1011840621111893):

1. The paper is copyedited by a professional copyediting service and some language corrections were made.

2. The protocol of this study was approved by Baskent University Institutional Review Board (Ref No: KA05/07). A statement to this effect is added in the Methods section of the manuscript. (Methods section, first paragraph, lines 6-7)

3. Abstract of the manuscript is re-structured according to the guidelines provided at the link: http://www.biomedcentral.com/info/ifora/abstracts

4. The title “Introduction” was changed as “Background”. The discussion section was divided and the last two paragraphs of this section were presented in the “Conclusion” section. The sections of “Competing Interests” and “Authors’ contributions” were added to the manuscript. Manuscript sections were reordered, as appropriate.
Our reply to the reviewer, Tim R Wolfe:

Minor Essential Revisions:

The reviewer stated that: “Please clarify these sentences -" The tip of the pump was streaked, and 0.01 mL of the fluid in the pump was inoculated on the agar surfaces. The inside of the pump was rinsed with 1 ml sterile distilled water..."Was the pump or the bottle cultured in this last sentence? From the study design it sounds like the bottle was cultured, but from this sentence and the prior it sounds like the inside of the pump was cultured twice.”

Our reply: In line with the comment by the reviewer, “and 0.01 ml of the fluid in the pump was inoculated” was removed from the sentence “The tip of the pump was streaked and 0.01 ml of the fluid in the pump was inoculated on the agar surfaces” (Methods section, paragraph 5, line 4) and added “A sample of the fluid that remained in the spray bottle was also cultured.” to the end of the paragraph. (Methods section, paragraph 5, line 7-8)

The reviewer stated that: 3rd sentence -reads "from 66 sprays" should read "from 66 spray devices"

Our reply: In line with the comment by the reviewer, "from 66 sprays" is corrected as "from 66 spray devices". (Results section, paragraph 1, line 4)

Discretionary revisions:

The reviewer stated that: “I think the Abstract could be slightly more specific and include a conclusion so the readers have a better understanding of the study and the conclusions of the authors. I would make the following changes to clarify the data: Sentence 1: Reusable nasal spray devices are frequently used in otolaryngology examination, and there is increasing concern about the cross contamination risk of these devices. Sentence 2: Rather than use "the
safety of these devices” I would state “the safety of a positive displacement, or pump, type atomizer "Sentence 3: Rather than "Nasal sprays were used...” I would say "Reusable nasal spray bottle, pump and tips were used.”I would add a conclusion to the abstract similar to the conclusion of the document discussion. Something like "Given these findings we conclude that additional precautions (such as autoclave between uses, disposable tips, or disposable devices) are warranted to avoid patient cross contamination from a re-usable nasal spray devices.”

Our reply: In line with the reviewer’s suggestions, the following changes were made in the abstract section:

- “Nasal sprays are frequently used in otolaryngological examination, and there is increasing concern about the cross contamination risk of these multi-use sprays” was changed as “Reusable nasal spray devices are frequently used in otolaryngologic examinations, and there is increasing concern about the risk of cross contamination from these devices.” (Abstract section, Background subsection, line 1-3)
- “the safety of these devices” was changed as “the safety of a positive displacement, or pump-type atomizer” (Abstract section, Background subsection, line 4-5)
- “Nasal sprays were used” was changed as “A reusable nasal spray bottle, pump and tips were used” (Abstract section, Methods subsection, line 1)
- “Given these findings we conclude that additional precautions (such as the use of an autoclave between sprays, disposable tips, or disposable devices) are warranted to avoid interpatient cross-contamination from a reusable nasal spray device.” was added as a conclusion to the abstract. (Abstract section, Conclusions subsection)

The reviewer stated that: “When discussing the Venturi effect and how it can create a "suck back” it might be appropriate to add a sentence at the end of the paragraph describing how the
fluid column sucked up by the Venturi effect collapses back into the bottle once the airflow ceases, resulting in a transient suction at the tip -that may aspirate material into the device.”

**Our reply:** In line with the reviewer’s comment a sentence of “The fluid column sucked up by the Venturi effect collapses back into the bottle after the airflow has ceased; this results in a transient suction at the tip that can aspirate material into the device.” was added into the discussion section. (Discussion section, paragraph 2, line 9-12)

**The reviewer stated that:** When discussing the Visosky article, you should consider contrasting their underpowered design (12 atomizers used on 40 patients in a two week time period with no positive cultures hardly provides statistical proof of lack of contamination risk).

**Our reply:** This comment of the reviewer was ignored as it was suggested as a discretionary revision

**The reviewer stated that:** “You might also consider adding discussion of the Dubin article - one with similar size and design to yours, but using a Venturi atomizer -and contrasting their conclusions to yours. You found a far smaller rate of contamination (2%) but conclude it is a problem, yet they found a 66% contamination rate in lidocaine bottles, but concluded that this was of questionable clinical significance. I think this contrast is the point of the debate and the controversy and exposes the whole point of your article. You clearly point out that it is a matter of discussion whether statistics or "numbers to treat" is the issue and are one of the few to conclude that it is unacceptable for even one MRSA (or other non-cultured organism) to be transmitted. This opinion and discussion could be expanded somewhat.”

Our reply: In line with the reviewer’s comment, a discussion of the Dubin article was added to the discussion section, as: “In a study of Venturi-type atomizers containing either lidocaine or tetrahydrazoline hydrochloride (Tyzine) that was applied with the aid of a nasal speculum to reduce contact with the skin and mucosa, Dubin and colleagues (10) showed that wiping the nozzle of the atomizers with an isopropyl alcohol pad after each use resulted in a significant reduction of contamination (from 66% to 6%) in the lidocaine-containing atomizers after 2 weeks; but that after 1 month no significant difference in the contamination rate between the wiped and nonwiped atomizers was noted. Those authors concluded that although a low level of contamination of multiuse Venturi atomizers might occur in practice, it is of questionable clinical significance and that wiping the tips of the devices with isopropyl alcohol between uses could eliminate microbial growth for a 2-week interval (10).”

(Discussion section, paragraph 5, line 14-26)

The reviewer stated that: “You found only contamination of your bottle tip, but conclude the entire device needs to be disposed. What not conclude that either the entire bottle or simply the tip needs to be disposed?”

Our reply: In line with the reviewer’s comment, “replacing the tip with a new sterilized one, after each patient, may be a practical and inexpensive alternative” is changed with “replacing the nozzle tip with a new sterilized tip after each use, or simply using disposable tips for each patient may be a practical and inexpensive policy” (Discussion section, paragraph 9, line 2-4). However, as mentioned in discussion section, (paragraph 9, line 6) the safety of this alternative needs to be proven with further studies, and no change was done in conclusion section.
**Our reply to the reviewer, Brent Senior:**

**Major Compulsory Revisions:**

**The reviewer stated that:**

1. It is important to recognize that MRSA is not coagulase negative staph. It appears that these are confused in the article and I would recommend that the authors clarify this.

**Our reply:** In line with the reviewer’s notice,

- “Although there was no statistically significant difference in positive culture rates among the groups, MRSA was isolated in 4 of 198 cultures.” was corrected as “Although there was no statistically significant difference in positive culture rates among the types of nasal spray bottles tested, methicilline-resistant coagulase negative staphylococci were isolated in 4 of 198 cultures.” (Abstract section, Results subsection, line 1-4)

- “With the fact that even one transmitted MRSA can cause a huge problem in certain patient groups, we can say that neither of the devices are acceptable” was corrected as “Because even 1 transmitted bacterium (or other non-cultured microorganism) can result in severe infection in certain patient groups, we suggest that neither of the devices in our study is acceptable” (Discussion section, paragraph 8, line 3-6)

**The reviewer stated that:**

2. In the methods, it is unclear as to how the uncapped bottles were cleaned. Is the 70% alcohol isopropyl alcohol, or 70% ethyl alcohol?
Our reply: In line with the reviewer’s suggestion, “Caps-off bottles were rinsed with 70% alcohol solution after each use” was changed as “Cap-off bottles (Figure 1) were rinsed with 70% ethyl alcohol solution after each use” (Methods section, paragraph 2, line 5)

The reviewer stated that:

3. No mention is made of institutional review board approval for this clinical study. Please tell the reader whether IRB was obtained.

Our reply: As it was mentioned above, the protocol of this study was approved by Baskent University Institutional Review Board (Ref No: KA05/07). A statement to this effect is added in the Methods section of the manuscript. (Methods section, first paragraph, lines 6-9)

The reviewer stated that:

4. Several references to Wolfe's papers are made that reflect negatively on venturi devices. It should be made clear to the reader that Dr. Wolfe has commercial interest in a disposable positive pressure application device.

Our reply: Dr. Wolfe’s conflict of interest has been acknowledged before, in the editorial comment on his paper “Wolfe TR, Hillman TA, Bossart PJ. The comparative risks of bacterial contamination between a venturi atomizer and a positive displacement atomizer. Am J Rhinol. 2002 Jul-Aug;16(4):181-6; discussion 186.” In addition, although they have made a reference to Dr. Wolfe’s same article, this kind of declaration was not done by Dr. Senior et al either, in their paper “Dubin MG, White DR, Melroy CT, Gergan MT, Rutala WA, Senior BA. Multi-use Venturi nasal atomizer contamination in a clinical rhinologic practice. Am J Rhinol. 2004 May-Jun;18(3):151-6/. Reference No: 4.” Declaring the commercial interest of the author of a given reference in the manuscript is thought not to be necessary, and this suggestion of the reviewer is ignored.
The reviewer stated that:

5. The discussion of how the venturi atomizer works is very good. I would recommend that this be contrasted as to how the positive pressure devices work and why they would be at theoretically lower risk of contamination.

Our reply: In line with the reviewer’s recommendation, a part on how the positive pressure devices work and why they would be at theoretically lower risk of contamination is added to the discussion section of the manuscript: “Positive displacement atomizers do not rely on the Venturi principle, but instead use the noncompressible properties of fluid to atomize medications. In positive displacement atomizers, manually applied kinetic energy is transmitted through a spring-driven pump system to the fluid and causes an increase in the pressure, thus increasing the potential energy of the fluid in the reservoir. The increase in potential energy in turn drives the fluid through the pump lumen and out of the tip. With the aid of a 1-way valve system that prevents the “sucking-back” of the fluid and/or a specifically designed air-filter system that prevents the buildup of negative pressure in bottle, the fluid does not flow back into the bottle. This design theoretically lowers the risk of contamination.”
(Discussion section, paragraph 2, line 12-23)

The reviewer stated that:

6. How many colony forming units of methicillin resistant coagulase negative staph were recovered? This will give the reader a good understanding of how significant the degree of contamination was.

Our reply: Colonies seen on the agar surfaces (positive cultures) were studied further, and the bacterial strains were identified by conventional laboratory methods; additional colony forming unit count was not performed. To make this clear to the reader, a statement of “additional colony forming unit count was not performed” was added to the methods section of the manuscript. (Methods section, paragraph 6, line 3-4)
The reviewer stated that:

7. I disagree with the conclusion on page 6: "with the fact that even one transmitted MRSA can cause a huge problem in certain patient groups, we can say that neither of the devices are acceptable." First, we do not know the clinical significance of coagulase negative staph growth to the patient. Second, is this a technique issue? Is it possible that better rubbing of the cap with alcohol, or use of a nasal speculum without skin/mucosal contact would eliminate the growth? In our review (Dubin, et al. AJR, 2004) we found no growth at one week with venturi atomizers wiped with isoproponal and applied with the aid of a nasal speculum to reduce skin/mucosa contact.

Our reply: This issue is discussed in the discussion section of the manuscript. We also added a discussion of the Dubin article. In that study, Dubin et al worked with Venturi type lidocaine and Tyzine atomizers that were applied with the aid of a nasal speculum to reduce skin/mucosa contact, and showed that wiping the nozzle of the atomizers with an isopropyl alcohol pad after each use had resulted in a significant reduction of culture-positive lidocaine atomizers from 66% to 6% after two weeks; but after 1 month no significant difference in contamination rate was seen between wiped and non-wiped atomizers. As the reviewer, we also do not know the clinical significance of coagulase (-) staphylococci growth to the patient. However, as stated at paragraph 8 of the discussion section, even 1 transmitted bacterium (or other non-cultured microorganism) can cause a huge problem in certain patient groups such as those who has immunodeficiency. Although statistically not significant, the fact is that the devices were shown to be contaminated. It is a matter of discussion whether “numbers to treat” or statistical principles should be used in evaluation of results like this. However, from our clinical point of view, this is adequate enough to take every precaution to prevent cross-contamination between patients, at least up to the time that the cross-contamination with any microorganism is proven not to be possible.