

Author's response to reviews

Title: Hospital-acquired Fever in Oriental Medical Hospitals

Authors:

Soo-youn Moon (sooyounmoon78@gmail.com)

Ki-Ho Park (parkkiho@hotmail.com)

Mi Suk Lee (mslee@khmc.or.kr)

Jun Seong Son (isonjs@naver.com)

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Author's response to reviews:

Background:

--The authors should provide a reference or further explanation for the following statement: "In Korea, patients with cerebrovascular accident and elderly patients tend to seek oriental medical care more often than other patients." I believe this is cited as #13 in the discussion.

→ I've provided a reference.

Methods:

--This is a minor comment, but the authors may wish to clarify that the IRB waived the requirement for informed consent. "Consent from the patients was waived," almost sounds as if patients waived their rights.

→ The sentence was changed to "Informed consent from the patients was waived by IRB."

--Suggest changing "infections" to "fever" in this sentence since, it seems, the study evaluates all fevers regardless of whether they were caused by infection. "If a patient was transferred from another OMH where he or she was admitted for more than 48 hours and where fever started within 48 hours of hospitalization, these ****infections**** were also considered hospital-acquired."

→ I've change the word "infections" to "fevers."

--The authors should clarify how they reviewed patients' records, since there were >11,000 patients. Was this done by manual review of each chart or via electronic records?

→ We have electronic medical records system which we used to find all in-hospital patients with fever. I've changed the sentence as below:

“Patients hospitalized in the OMHs from June 2006 to June 2013 were retrospectively reviewed via electronic medical records by two infectious diseases specialists.”

--The authors should clarify who adjudicated whether the CDC infection criteria were met and with what data (again, manual chart review vs. electronic records vs. infection control department records, etc.).

→ Two infectious diseases specialists review the charts and adjudicated the cases according to CDC criteria.

--The authors should also clarify who determined fever attribution and specific data sources (see above).

→ We have electronic medical records system which we used to find all in-hospital patients with fever. I've changed the sentence as below:

“Patients hospitalized in the OMHs from June 2006 to June 2013 were retrospectively reviewed via electronic medical records by two infectious diseases specialists.”

Results:

--I'm not an expert in this area but I wonder how the authors can confidently attribute 7 and 1 cases of fever to moxibustion and cupping, respectively. Is it possible that these fevers had some other unidentified etiology?

→ These patients had fever during the procedures, but when the procedures were stopped for several days, they had no fever. Also there was no evidence of infection or other causes of fever.

--The paragraph describing Table 3 is very hard to follow and repeats information that is in the table. Suggest cutting this down significantly.

→ The paragraph was revised and reduced the repeated informations.

--In Table 3, the Ns for some of the conditions (e.g., hematologic malignancy and chronic kidney disease) are too small for comparisons by Chi-square to be appropriate. Since the numbers are so small it may not be meaningful to include these.

→ Some data are excluded from the table.

--In Table 3, some of the "comorbid conditions" really are interventions (e.g., receipt of various therapies). Suggest changing the subheading.

→ Subheading of "concurrent treatment" is added.

--In Table 3, were the laboratory findings obtained before or after the onset of fever? If after, these would more appropriately go in Table 4 because they would be clinical outcomes of fever, not causes. The authors should specify either way. **Importantly, if WBC is measured during/after onset of fever, it cannot be a risk factor for febrile illness and must be removed from the analysis in Table 5.

→ The lab findings in table 3 were at the onset of fever. And the subheading was specified. WBC is not a risk factor for infection, rather, associated factor for decision criteria for infectious cause of fever.

--Table 5 is slightly confusing. Is it the case that all of the factors under both subheadings were included in the same model and the authors flipped the direction of the ORs under "non-infectious" to be easier to interpret? Or are these two separate models? Personally, I think it is more intuitive to show the ORs going in the opposite direction (i.e., >1 vs. <1)—especially if these came out of the same model (which they should have).

→ They were 2 separate models. But, as you've mentioned, I did the multivariate analysis again and changed the table.

--In Table 5, it is not clear how the authors determined which factors would be included in the model. Presumably there is a p-value cutoff from Table 3 but this should be noted.

→ Factors with statistical significance from table 3 were chosen for multivariate analysis. I've added this in method.

Discussion:

--The authors note that, "In OMHs, more patients with solid cancer (55.9% vs. 32.9%, $p < 0.001$) and history of anticancer chemotherapy (31.3% vs. 12.1%, $p < 0.001$) have non-infectious fever. In these patients, moxibustion was more commonly used, and herbal medication was less commonly prescribed. Moxibustion was more commonly used in the non-infection group, while herbal medicine was more frequently prescribed to patients in the infection group." If this is so, it would be important to include these therapies in the multivariable model in Table 5.

→ Unfortunately, there was no statistical significance and even when they were included in the multivariate model, there was no meaningful ORs. So I did not put them in Table 5.

Conclusion:

--"In this study, incidence of nosocomial fever was not higher in OMHs..." The authors need to specify what they are comparing to. Data from other studies of Western medicine hospitals? If so, repeat references here.

→ The references were inserted in the sentence.

-- "...Herbal medicine was the most common cause of drug fever and invasive oriental medical procedures caused procedure related fever more frequently than Western medical procedures in OMHs." I don't think data are presented to support either of these conclusions. If this is the case, please break down the data in a way that supports these conclusions.

→ There were some data not mentioned in results so, I added them to the results and discussion.

Among 101 patients with drug fever, herbal medicine was the most common cause (95 cases, 94.1%), while antibiotics or bisphosphonate were the cause of drug fever in 6 patients.

Overall incidence of procedure-related fever caused by invasive oriental procedures is 2.9% (16 episodes), while incidence of procedure-related fever caused by western medical procedures is 1.4% (8 episodes).

Procedure-related fever in Western medicine was about 1.5% to 5.9%, [2, 7] while incidence of procedure-related fever in our OMH was 4.2%, which was not different from other studies.

Among the procedure-related fever in our OMH, fever related to invasive oriental procedure was higher than that related to western medical procedures (2.9% vs. 1.4%).

Editorial comments:

--The table abbreviations are for short terms (e.g., HTN for hypertension) and seem unnecessary.

→ The table abbreviates for short terms were removed.

--HAF and nosocomial fever are used interchangeably throughout. If an abbreviation is defined it should be used consistently. Personally it is easier to read as "nosocomial fever" since this term is short. Either way, should be consistent.

→ For consistency, I have changed "Nosocomial fever" to HAF.

--Decimal points for percentages are not consistent in the text (ones place, tenths place, hundredths place all are used).

→ In the discussion, the decimal points for percentages are not consistent, because some numbers are from other studies. I've changed them to be consistent with our results.