Author’s response to reviews

Title: Association between Environmental Particulate Matter and Arterial Stiffness in Patients Undergoing Hemodialysis

Authors:

Cheng-Hao Weng (drweng@seed.net.tw)
Ching-Chih Hu (nonahu5248@gmail.com)
Tzung-Hai Yen (m19570@adm.cgmh.org.tw)
Wen-Hung Huang (willammedia@yahoo.com.tw)

Version: 1 Date: 24 Aug 2015

Author’s response to reviews:

Reviewer #2:

Weng CH et al. had evaluated the association of environmental particulate matter on arterial stiffness in hemodialysis (HD) patients, and found environmental PM10 level is associated with baPWV. The topic is interesting, however, there are some issues needed to be addressed.

Major:

1. The authors should acknowledge the difficulty in determining direction of causality in the relationship between arterial stiffness and environmental particulate matter. Does environmental particulate matter cause arterial stiffness? This study is just a cross-sectional study. The authors should avoid the words of "impact" or "effect".

   Ans: We have changed and avoided the words of “impact” or “effect” in the Title and content of the manuscript.

2. What is the definition of "abnormal baPWV"? The authors should put the cut point of abnormal baPWV in the Methods and Table 3.

   Ans: We have put the cut point in the Methods and Table 3.

3. MAP (distending) pressure is widely recognized to be a determinant of arterial stiffness and so adjustment for this should be made prior to testing for univariate correlation. Adjustment was performed by a linear regression of the two variables. The residual
values were then added to uncorrected baPWV to form the adjusted baPWV. Adjusted baPWV values were then used for analysis.

Ans: We have adjusted baPWV by MAP and recalculated the linear regression of MAP adjusted baPWV and all the parameters.

4. Besides, heart rate is an obvious determinant of arterial stiffness—The authors should put heart rate into multivariate analysis for adjustment.

Ans: We have added heart rate into multivariate analysis for adjustment.

5. How about the medication, especially anti-hypertensive drugs? The authors should put anti-hypertensive drugs (ACEI/ARB, b-blockers, CCB) into multivariate analysis for adjustment

Ans: We have used univariate linear regression for ACEI/ARB, beta blocker, and CCB. In univariate analysis, they all did not showed stastically significant (as showed in Table 3.)

6. The time of the measurement of ABI is important, before HD? after HD? Interdialytic HD? Besides, the date of the ABI measurement and environmental PM check and blood collection should be addressed on the Methods.

Ans: The HD patients were measured one hour before HD. The date of baPWV measurement and blood collection were addressed in the Methods.

Minor:

1. The abbreviation should be used after full name use in the manuscript.

Ans: We have checked and use full name before the use of all the abbreviations

2. Data for triglyceride, iPTH, aluminum and hsCRP are skewed, and should be log-transformed for analysis.

Ans: We have used the log-transformed TG, iPTH, Al, and hsCRP for analysis.

3. Table 2 is not necessary.

Ans: We have deleted Table 2.
4. Please show univariate analysis of "all" variables in Table 4, not just significant variables. I am surprised that albumin was not associated with baPWV.

Ans: We have listed univariate analysis of all variables in Table 3 (previous Table 4)

Reviewer #3:

The authors are obviously experienced in studying air pollution and surrogate outcomes among end-stage renal disease patients and published papers in this area. In the current project, they access the correlation of air pollution variables and PWV in patients undergoing hemodialysis and concluded air pollution parameter PM 10 is positively associated with baPWV measurement among dialysis patients. I have several concerns to this article, mainly on study design.

Major:

1. The author compared pulse wave velocity in their "hemodialysis patients" but used a reference data from "healthy people". they concluded 16 of their patients had normal baPWV and 111 patients had abnormal values. I think they used a wrong reference data because most end-stage renal disease patients have vascular calcification; these patients obviously have extremely stiff vessels and abnormally high baPWV measurements. Their data also showed gender, DM and hypotension all affect the bpPWV 10~20 times higher than PM 10 in this patient population (Table 4).

Ans:

1. Because there was no previous data to show the normal range or average range of baPWV in dialysis patients, the normal (within the distribution of PWV) or abnormal (higher than the distribution of PWV) of PWV was based on the study by The Reference Values for Arterial Stiffness’ Collaboration.

2. Although gender, DM and hypotension all affect the bpPWV 10~20 times higher than PM10 in this patient population. But PM10 is a novel predictor of baPWV in HD patients in this study, so we focused on the effect of PM10 on baPWV of HD patients.

2. The authors correlated the air pollution level and baPWV measurements in hemodialysis patients from a single center. I assume these patients located near by the hospital and the air pollution level among each patient was similar. I suggest the authors collaborate with other centers and expend the patient number and more importantly, compare the baPWV results between patients live in area with heavy and less air pollution.
Ans: Our hospital is one of the largest medical centers in Taiwan located in Kwei-Shan, Taoyuan, Taiwan. Many of our HD patients came from the New Taipei City and Taoyuan city. The distance between their hometown and our HD center is usually more than 10KMs. And the air quality is different even between nearby towns, such as Taoyuan and Zhongli districts in Taoyuan city (http://taqm.epa.gov.tw/taqm/en/default.aspx). However, the reviewer’s suggestion is good and we will try to collaborate with other centers in the future studies.

3. The author analyzed the association between a single baPWV measurement and a 365 day-mean air pollution level, I am not sure this is a correct method. Does the air pollution severity consistent in Taiwan through the whole year? Or the air pollution is more severe in some season than others, and therefor the baPWV measurement changes seasonally?

Ans: We have used the same method in our previous studies (Medicine (Baltimore). 2015 Jan; 94(1):e368, Medicine (Baltimore). 2014 Nov; 93(26):e181, and Medicine (Baltimore). 2014 Nov; 93(25):e149). But the suggestion of the reviewer is good and we will try to analysis the baPWV in different seasons with different severity of air pollution.

Minor:

1. If the authors decide to revised this article, they need to send it for English editing, there are many grammar errors and typos. The authors also used many abbreviations in this article for the readers. I suggest the authors clarifying what this abbreviation stands for before use them. (For example, "Al", "baPWV" in introduction,

Ans: We have sent for English editing and clarify what abbreviation stands for before use them.

------------------- Editorial Requests -------------------

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If your study involves humans, human data or animals, then your article should contain an ethics statement which includes the name of the committee that approved your study.
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Consent: If your article is a prospective study involving human participants then your article should include a statement detailing consent for participation. If individual clinical data is presented in your article, then you must clarify whether consent for publication of these data was obtained.

Ans: We have clarified that consent for publication was obtained in the manuscript. Availability of supporting data: BioMed Central strongly encourages all data sets on which the conclusions of the paper rely be either deposited in publicly available repositories (where available and appropriate) or presented in the main papers or additional supporting files, in machine-readable format whenever possible. Authors must include an Availability of Data and Materials section in their article detailing where the data supporting their findings can be found. The Accession Numbers of any nucleic acid sequences, protein sequences or atomic coordinates cited in the manuscript must be provided and include the corresponding database name.

Ans: We have added the section of Availability of Data and Materials. And because we do not have publicly available repositories, the original data set can be obtained by mailing the request to our first author (Cheng-Hao Weng, drweng@seed.net.tw) or corresponding author (Wen-Hung Huang, williammedia@yahoo.com.tw) Authors Contributions: Your 'Authors Contributions' section must detail the individual contribution for each individual author listed on your manuscript.

Ans: We have added 'Authors Contributions' section which detailed the individual contribution for each individual author.