

March 18, 2014

Dear Editor,

Please find attached our manuscript in Word format (file name: 8244 - Revised Manuscript.docx) entitled 'Antihypertensive drugs and glucose metabolism' revised according to the editorial office recommendations and the reviewer's comments. All changes are highlighted in yellow in the revised text. At this point we would like to thank the editorial office and the reviewer for their kind comments.

Title: Antihypertensive drugs and glucose metabolism

Author: Christos V. Rizos, Moses S. Elisaf

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 8244

Specifically,

According to the Editorial Office comments:

1. Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

A summary of less than 100 words to outline the most innovative and important arguments and core contents in our paper has been added (page 2; lines 22-31).

According to Reviewer 1 comments:

1. The authors, in fact, choose some categories of drugs that do not affect glucose metabolism in the treatment of hypertension : inhibitors of angiotensin and ARBs.

The purpose of our manuscript was to evaluate the various antihypertensive drugs in respect to their capacity to influence glucose metabolism. We chose to review all the common antihypertensive drugs and explore their effect on glucose homeostasis whether this effect was beneficial, neutral or detrimental. The majority of clinical studies have identified that both angiotensin receptor blockers as well as angiotensin converting enzyme inhibitors have overall a beneficial effect on glucose homeostasis. However, we have also presented in the manuscript studies that have shown neutral effect of the above drug categories on glucose metabolism.

2. An insignificant effect was attributed to calcium antagonists (and this is only partly true , because the favorable effects of this class of drugs on glucose metabolism have been observed !)

The class of calcium channel blockers is considered overall as having neutral effect on glucose metabolism. We agree that some members of the class (i.e. amlodipine and nifedipine) have a beneficial effect on glucose homeostasis and we present relative studies as well as possible mechanisms for their effect in the manuscript. We now have also added this differentiation of amlodipine and nifedipine in the abstract (page 2; lines 8-11) as well as the conclusion section of the manuscript. (page 16; lines 16-17).

3. While strict contraindications would be attributed to beta blockers. This is true when one does not consider the positive effects of these drugs on other metabolic parameters and , above all, the final result obtained in reducing the incidence of other complications of hypertension.

A number of studies have shown that the overall effect of β -blockers on glucose homeostasis is disadvantageous. However, we present in the manuscript that

some members of the class (i.e. carvedilol and nebivolol) have a more attractive profile regarding glucose metabolism. We agree that despite the negative effects of β -blockers on glucose homeostasis, the overall expected benefits versus the potential risks should always be carefully weighted for each individual patient as stated in the conclusion section. Furthermore, we now indicate that patients required to receive a β -blocker or a diuretic should not be disqualified because of the negative effect that these categories have on glucose homeostasis (page 17; lines 33-35).

We do hope that the revised manuscript now meets your requirements.

Thank you again for publishing our manuscript in the World Journal of Cardiology.

Sincerely yours,

Yours sincerely,

A handwritten signature in blue ink, appearing to be 'Moses Elisaf', with a stylized, cursive script.

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