Format for ANSWERING REVIEWERS

August 25, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 3482-review.doc).

Title: Vascular response to vasodilator treatment in microalbuminuric diabetic kidney disease

Author: Narisa Futrakul, Prasit Futrakul

Name of Journal: *World Journal of Nephrology*

ESPS Manuscript NO: 3482

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Response to reviewer 00503274

1. Table 1 represents the unpublished renal function and intrarenal hemodynamic studies in microalbuminuric diabetic kidney disease. Microalbumin / creatinine ratio confirms the microalbuminuric stage of diabetic kidney disease. Fractional escretion of magnesium is a tubular function marker which is abnormally elevated reflecting the presence of tubulointerstitial disease. It is also abnormally elevated before any evidence of microalbuminuria (Renal Failure 2011; 33:312-325). Therefore, we consider that it is more sensitive biomarker than microalbuminuria.
2. In introduction-line 2, we agree with the reviewer that serum creatinine is not a sensitive diagnostic marker for diabetic kidney disease; however many clinicians or even nephrologists still use it as a screening tool for kidney disease. With respect to microalbuminuria, it is generally accepted to be a biomarker for screening diabetic kidney disease. However, it does not recognize a majority of early stage diabetic kidney disease, by which it has left most of these unfortunate early stage diabetic kidney disease patients unattended and allows them to progress toward a greater impaired renal function. Evidence-based information renders support that this early stage diabetic kidney disease is associated with an adequate vascular homeostasis and is vulnerable to respond to vasodilator treatment. Treatment with vasodilator at this early stage (normoaluminuria) can enhance renal perfusion, as well as restore renal function.
3. We agree to change as per the reviewer suggestion.
4. We agree to change in accordance with your suggestion.
5. We agree to change in accordance with your suggestion.

6. Defective angiogenesis and an impaired nitric oxide production induced by a variety of circulating toxins such as oxidative stress, sugar, lipid, cytokines etc, would eventually injure the renal microvessel and induce the progression of renal microvascular disease and chronic renal ischemia which inversely correlates with the magnitude of tubulointerstitial fibrosis.
7. We agree to change in accordance with your suggestion.
8. Calcium channel blocker has been added to some of the patients for controlling of the blood pressure.
9. We agree to change to fractional excretion of magnesium.

Response to reviewer 00503218

1. There is evidence to support that diabetic nephropathy can be recognized even in the early stage before any evidence of microalbuminuria (Futrakul Renal Failure 2011; 33:312-315, Ritt Am J Kidney Dis 2009; 53:281-289). Treatment at this early stage (normoalbuminuria) can enhance the renal perfusion an restore renal function. But treatment at later stage can simply slow the renal function but cannot restore the renal perfusion.
2. We are that diabetic nephropathy has its own stage system.
3. We have updated the publication hemodynamic study.

Response to reviewer 00503173

Thank you for your suggestions, we have changed in accord with your comment.

3 References and typesetting were corrected

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

Sincerely yours,
Dr. Narisa Futrakul,
Faculty of Medicine,
King Chulalongkorn Memorial Hospital,
Chulalongkorn University,
Phayathai Road,
Pathumwan, Bangkok 10330, Thailand.
Fax: +66-2-2564911
fmednft@yahoo.com