Author's response to reviews

Title: Urine alkalization facilitates uric acid excretion.

Authors:

Aya Kanbara (achan@gaines.hju.ac.jp)
Masayuki Hakoda (hakoda@yasuda-u.ac.jp)
Issei Seyama (seymai@gaines.hju.ac.jp)

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Author's response to reviews: see over
Dear Dr Liebman:
Thank you very much for your succinct and critical comments given to our paper. Following descriptions are the point-by-point responses to your suggestions.

Major compulsory Revisions
1. To answer your question, we would like to revise Fig 3 in old text to new Fig 3, in which data for uric acid excretion are presented as the absolute values per day. Since we used the same food materials through 5-day study, data for creatinine excretion during 5-day study were relatively stable.
2. We do wish to know serum uric acid concentration. Unfortunately, this experiment was done in a woman’s university campus without the help of medical staff. This difficulty precluded us from collecting the data you suggested to get. However, it seems to me that the lack of these data does not hurt the significance of this work. Since there are many reports that oral purines and nucleotides increase uric acid concentration in plasma as well as in urine in dose-dependent manner, and the amount of intake of purine body from the acid diet is calculated to be bigger than that from alkali diet as mentioned in text, one can expect that uric acid excretion in acid diet would have been more than that in alkali diet in this study. Results obtained were just opposite, suggesting that there may be urine pH-dependent transport systems in the human kidney.

We will appreciate very much, if you permit us to report serum uric acid data in the next paper.

According to Waring et al (2001) in J Cardiovascular Pharmacology 38:365-371, 1000mg uric acid loading over 60 min increased serum uric acid by 5mg/dl. If one simply applies our data of increased removal of uric acid by 100mg/d in alkali urine and ignores time dependent factor, decrease of serum uric acid by 0.5 mg/dl could be induced. Since we do not know time-dependent factor of uric acid removal and urine acid pool in our case, we can not anticipate a reasonable value. Thus, we do not want to describe this information in our paper.

3. We agree with you and delete this last sentence, because we explained the significance of this study in terms of the effect of evolutionary change in diets on kidney function enough.

Minor essential revision.
1. We explained the experimental procedure more precisely in the method section. We hope this additional statement will eliminate your concern.
2. We change the word “always” to “sometimes” and the original sentence “it is worthwhile········” to your suggestion “alternative way········”.

3. We delete the section discussing “uric acid urolithiasis” (p9 L6-L8 from bottom).

4. We put the explanation of shapes in Fig.2.

5. We use “significantly” in stead of “exponentially”

6. We replace colloquial word of “As a matter of fact” with “actually”.
Dear Dr Malaguarnera:
Thank you very much for your succinct and critical comments given to our paper. Following descriptions are the point-by-point responses to your suggestions.

Answer to your request in Background
The papers you suggested to cite not only stirred up our scientific interest, but also impressed us how widely our work may be associated with resolution of pathological conditions. However, it seems to us that uricase application is in preliminary stage, because clinical problems of immune response caused by its long time use still need to be overcome. Therefore, this time we are unable to cite references you requested.

Answer to your point in Subjects.
In order to incorporate your suggestion, we add the statements female students (21-22 years old, 45-60 kg in body weight and 157-170 cm in height) who had no health problems in the physical checkup conducted by the University.

Answer to your suggests in Methods.
Since our sample data are reasonably assumed to be in the normal distribution, we use parametric analysis instead of nonparametric techniques you suggested to use.

Answer to your point in Discussion.
In order to incorporate your suggestion, we insert new phrase “in much economical way” into the Conclusion section.
As long as we pay attention to constructing the nutritionally balanced menu for alkali diet, we think we will have little side effect.
Dear Dr. Doughty:
Thank you very much for your critical reading and succinct and productive comments given to our paper. Following descriptions are the point-by-point responses to your suggestions.

Answer to your first suggestion.
In the discussion section, we newly cite two papers of Griebsch and Zöllner (1974) and Clifford et al. (1976), in which oral purines increases uric acid concentration in serum as well as in urine in dose-dependent manner. Our result is just opposite to what we expected from their results. We believe that there may be pH-dependent uric acid transport in human kidney and because of this characteristics, we can recommend for patients with gout to eat low protein diet.

Answer to your second suggestion.
To make clear the data presentation procedure, we add the sentence “which were obtained by averaging data of...”.

Answer to your third suggestion.
Although there are many suppositions that the mismatch between our genetically determined nutritional requirement and our contemporary diet causes many contemporary health problems, a few of them are verified by definite examples. This report, we think, is an additional example of the mismatch, showing that diet-induced mild acid urine generates the suppression of uric acid removal in the kidney. Therefore, we hope this section leaves in this form.

Answer to your fourth suggestion.
To respond your constructive suggestion that the same type experiment should be done in patients with gout, we will plan to do it. We hope to report the results to you near future. Thank you for your interesting proposal.