Reviewer's report

Title: Association between Na+K+-ATPase activity and some lipid metabolites in insulin dependent diabetic patients from Lagos, Nigeria.

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Reviewer: thierry coste

Reviewer's report:

General

In this study, the authors have investigated the relationship between red blood cell Na+/K+-ATPase activity and blood lipids in insulin dependant diabetic patients (IDDM). As expected, the Na+/K+-ATPase activity was decreased in IDDM patients when compared to control. Moreover, this enzyme activity was lower in the patients with poor glycemic control and its activity seems correlated with pro-atherogenic blood lipids.

This paper is potentially interesting since relationship between Na+/K+-ATPase activity and blood lipid parameters was poorly studied in IDDM patients. However, the manuscript presents some major concerns. Some important points need to be clarified or changed to strengthen the paper. Lastly, a lot of minor errors need to be addressed throughout the text.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1/ Introduction:
- In first paragraph, is Diabetes Mellitus “arising from” or “inducing” alterations in carbohydrate, lipid and protein metabolism?
- In second paragraph, Na+/K+-ATPase is active as a dimeric form (? and ?) and ? is present only in some specific tissues. Moreover, the third sentence is difficult to understand (a verbal form is required).

2/ Materials and Methods:
- There is a serious concern about the determination of erythrocyte Na+/K+-ATPase activity. Firstly, please precise if the ATP used was vanadate-free (an inhibitor of Na+/K+-ATPase). Secondly, what the authors defined as the total Na+/K+-ATPase activity was in fact the total ATPase activity (merely Na+/K+-ATPase activity + Mg-ATPase activity, see review from Steck TL in J Cell Biol 1974 or paper from Marchesi VT & Palade GE in J Cell Biol 1967). So, the Digoxin sensitive total Na+/K+-ATPase activity is the real total Na+/K+-ATPase activity. Moreover, the dose of digoxin used to inhibit Na+/K+-ATPase seems lower for me (700 nM). Usually, to assess the Na+/K+-ATPase activity in human erythrocyte, concentrations between 0.1 to 1mM of ouabain were used (see papers from Raccah D et al.).
- The values for HbA1c would be more accurate to assess a longer poor glycemic control in the A1 group versus A2 group if they are available…
This section should be seriously revised...

3/ Discussion: major revisions are required.
- In the first part, the advanced glycation hypothesis could be strongly supported if one correlation between Na+/K+-ATPase and HbA1c from your patients was available.
- In the second part, a reading of two papers from Konukoglu D et al. in Clin Invest Med 2003 and Uyuklu M et al. in Clin Hemorheol Microcirc 2007 and the review from Zicha J et al. in Am J Hypertens 1999, could be helpful in order to improve this part.
- Concerning the Na+/K+-ATPase activity, there is some confusion in this part (see comments above in the Materials and Methods section). In your ATPases assay, you used a calcium-free buffer so the calcium dependent-magnesium ATPase was inhibited. However, the magnesium ATPase (non calcium dependent) was not inhibited so the total ATPase activity was the sum of sodium potassium ATPase and also the magnesium ATPase. Please clarify and addressed that.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author
can be trusted to correct)

1/ The beginning of title could be changed to “Association between erythrocyte Na+/K+-ATPase activity and some blood lipids in insulin...”.

2/ In Abstract, there are some few minor errors to be addressed. For example, use “atherogenic” instead of “arterogenic” and “Friedewald formula” instead of “Friedwald formular”. Please clarify the second part of the conclusion sentence.

3/ In Introduction:
- For references, use [] or () consistently throughout the text.
- First paragraph, “involving” instead of “to involve”, remove “cell” after “nerve”, “affected by degenerative complications” instead of “which manifest diabetic complications”.
- Second paragraph, avoid “derangements” (prefer alterations, dysfunctions, etc.).
- Third paragraph, “susceptible” instead of “susceptibility”. “microalbuminuria” instead of “microalbinuria”.

4/ In Materials and Methods, page 7 “Friedewald” instead of “Friedwald”. Page 8, are you sure that the volume of Na+/K+-ATPase activity assay was 500 mL?

5/ In Results:
- First paragraph “No significant differences were noted between...” instead of “No significant (P > 0.05) between...”.
- Second paragraph, please avoid repetition of values and for the Tables 1 and 2, use the international units for biological analysis (a lot of them are listed in this web page: http://www.chups.jussieu.fr/polys/biochimie/usualval.html). In the last sentence, percentages are not the same than in table 2???
- Third paragraph, see related discussion in the major revisions concerning Materials and Methods. Avoid repetition of values from Table 3: please use preferentially sentences as “further analyses revealed a significant 30% increase in Na+/K+-ATPase activity in IDDM patients with good...”
- Fourth paragraph, the values for Vmax and Km are different in the text when compared with the box of Figure 1. Moreover, in Figure 1 title use “control” instead of “normal”.

6/ In Discussion, some typing errors should be addressed. Page 13, “14 of the 22 patients investigated”, should be “14 of the 34 patients investigated”.

7/ In References section, the authors should check carefully the references to correct some minor errors. For example, in reference 29 “Friedewald” instead of “Friedwald” and “ultracentrifuge” instead of “ultracentrifugation”.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests