Reviewer's report

Title: Skin-impedance in Fabry Disease: A prospective, controlled, non-randomized clinical study

Version: 2 Date: 3 March 2008

Reviewer: Robert D Steiner

Reviewer's report:

This manuscript reports the results of testing skin moisture content in patients with Fabry disease. While the report contains interesting data, the interpretation of the data and discussion of it in the context of previously published related reports of measurements of sweating in Fabry disease needs improvement, and the manuscript is further adversely impacted by a lack of clarity in presentation.

Major Compulsory Revisions:

The authors write in the abstract that skin impedance testing is useful for the clinical evaluation of Fabry disease without presenting data to support that statement and without clarifying why it is useful and how it should be used.

There is no support for the statement in the abstract that serial measurements of induced sweating may demonstrate a better effect of enzyme replacement therapy, this appears to be conjecture and has no place in the abstract as written.

In the results section, the authors write: â##All created outcomes â#|showed similar significant differences (p<0.0001) in skin-impedance values between the three groups of subjects for most test-sitesâ##. This statement would seem to imply that skin impedance was different in all 3 groups, ie ERT vs not ERT Fabry vs. controls. Yet, in Figure 3 skin impedance of ERT and non-ERT Fabry look the same, and the legend for Figure 3 suggests no differences between ERT and non-ERT Fabry. Also, in the discussion, impedance is said to be no different between ERT Fabry and ERT naïve Fabry patients. The figure should be modified to clearly show which values are significantly different.

That statement about GALA enzyme levels in subjects mirroring patient group membership and being statistically related and that patient group and enzyme level were similarly related to skin-moisture value is not supported by the data presented.

The authors suggest that serial measurements will likely be more helpful than static measures, but go too far in suggesting without any data that serial measurements may determine the frequency of ERT for Fabry disease since there is no evidence that serial measurements would demonstrate a change in impedance after infusion.
It is clarified that the DDIM system assesses the base level of skin-moisture and not induced moisture (sweating), but it should then be discussed the merits and/or pitfalls of measuring base skin moisture vs. induced moisture in Fabry disease. Which measurement is valid? Which reflects best the pathophysiology? Clarify also whether the DDIM system is a measure of sweating.

The investigators conclude that the current results are consistent with previous studies of TST and QSART in Fabry. In what way were they similar if the TST/QSART studies showed improvement in sweating with ERT but the DDIM system does not?

A discussion of additional studies to help determine whether ERT leads to epidermal nerve regeneration, a functional improvement in sensory nerves and ganglia, or to recovery in other components of the nervous system is included, but ERT didn’t improve impedance in this study, so this discussion would appear to be inappropriate in the context of results presented in this study.

Minor Essential Revisions

Table 3 is not interpretable by the reader who is unsophisticated in statistics and should be deleted.

What is being depicted in Figure 2 is not explained well enough for the average reader to understand the meaning and implications of this figure. Either explain what is in the figure and justify the need for this in the manuscript or delete it.

The sentence in the discussion: “Skin-impedance is significantly decreased in Fabry disease but shows no improvement either before enzyme infusion or two days post-infusion in a group of patients who received ERT for 3 years” is difficult to understand. It would be better to write, if this is the intended meaning, that impedance shows no improvement either 2 weeks after infusion, or 2 days after infusion.

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: Acceptable

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