Reviewer's report

Title: Lipoprotein lipase in hemodialysis patients. Extensive depletion of tissue stores by a low molecular weight heparin, despite low plasma levels of the enzyme

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Reviewer: Marc T Hamilton

Reviewer's report:

General
This paper can make a valuable contribution to those clinicians using heparin and substitutes and I have no major compulsory revisions, but I do have several constructive suggestions.

1. Nasstrom et al. report on the effect of low molecular weight heparin on plasma LPL activity and plasma triglyceride concentration in patients undergoing hemodialysis. This clinical study is of interest for those undergoing hemodialysis because conventional heparin infusion, while an effective anticoagulant, results in elevated plasma triglyceride concentrations after several hours of dialysis which may promote atherogenic processes. The title of the paper says "... extensive depletion of tissue stores by a low molecular weight heparin, despite low plasma levels of the enzyme." There are no direct measurements of tissue LPL and the authors said that the modest rise in plasma triglyceride concentration from 2-4 hours post initiation of low molecular weight heparin indicates a depletion of tissue LPL activity. Based on the plasma triglyceride concentration measurements the authors further conclude that "this depletion is at least as marked after dalteparin as after conventional heparin..." This paper could be significantly improved by either a direct measure of some tissue LPL and/or an indication of the effect of dalteparin and heparin on LPL efflux/turnover in some animal model.

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

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
2. Title: "Extensive tissue depletion" was not measured and no indirect measures of LPL efflux/turnover were made. Thus, it is bold to state in the title that something is happening when there is no direct evidence this is true. However, I understand the argument being made from the present data, as well as the published work using a second heparin bolus. The argument for tissue depletion is logical, and I agree that tissue LPL is probably depleted by any type of heparin. This has practical ramifications for clinicians. Thus, considering another title that could more accurately conveys what was found in this study should be considered.

4. Page 2. Are there any studies in animals showing that LMW heparin affects LPL clearance? If so, this would help your argument greatly.

Discretionary Revisions (which the author can choose to ignore)
5. Abstract –The final paragraph discusses other studies and not the data from this present study. If that is to be retained, perhaps it would be simple to state "in prior in vitro studies...".
Background
6. Page 2. Line 4. Remove the bolded word “ref” since it is not useful.
8. Page 2. Lines 22-23. Was the LMW heparin infused at the same absolute dose (molar heparin concentration) or the same effective dose for anticoagulation as conventional heparin?

Results and Discussion
9. It is said in the Discussion that from 2 hours on, the TG concentration with LMW heparin increases significantly, although this is not shown in a very compelling way in the results.

10. One conclusion is that there was a time by treatment interaction revealing increased TG concentration with LMW heparin vs conventional heparin. Authors should be aware that a paired Wilcoxon sign rank test is for comparing two individual data points and your credibility could be improved if there some kind of correction for multiple time point comparisons, and a non-parametric test that would be analogous to the parametric 2 way repeated measures ANOVA where there are two factors (time and treatment).

11. Page 4. 2nd paragraph. There was a significant 32% increase in total cholesterol during dialysis. Could this be used too to strengthen the Discussion and conclusion that LMW heparins disturb lipid metabolism. HDL-cholesterol was not changed, so was there an unreported increase in LDL cholesterol.

12. The conclusion that tissue depletion is at least as marked as after dalteparin as after conventional heparin is not measured. Because plasma TG concentrations increase more under dalteparin this does not necessarily mean that TG clearance is more reduced under dalteparin compared to heparin. Concentration of TG is under the influence of not only clearance but also production. Also, the lower plasma LPL activity after dalteparin could be due to slower release of LPL activity from tissue than during heparin. In fact, the more significant drop in TG in the early part of the heparin trial could support this. Thus, the authors’ could more clearly and completely describe their previous paper using healthy individuals where they concluded “dalteparin and conventional heparin had reduced the peripheral stores of LPL to a similar extent and that the difference in plasma levels of LPL activity was due to a more rapid hepatic clearance of the LPL-dalteparin complex.”

What next?: Accept after minor essential 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

Declaration of competing interests:

NONE