Reviewer's report

Title: Lipoprotein lipase activity and mass, apolipoprotein C-II mass and polymorphisms of apolipoproteins E and A5 in subjects with prior acute hypertriglyceridaemic pancreatitis

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Reviewer: Emilio Ros

Reviewer's report:

This paper compares a group of patients with past hyperlipidemic acute pancreatitis (AP) with a group of patients with similar triglyceride elevations but no history of AP for clinical features, lipoprotein and apolipoprotein levels, LPL mass and activity, apoE genotype and a relevant apoA5 polymorphism. There are not many relatively large series of hyperlipidemic AP in the literature, and the biochemical and genetic studies performed here are important. The main message is that severe LPL deficiency is not a common cause of hyperlipidemic AP, but is still identifiable in a substantial minority of patients.

Major compulsory revisions

1. The series seems is biased towards male patients with moderate alcohol drinking and might include cases of alcoholic pancreatitis. Alcohol consumption is critical, as some “moderate drinkers” (what does it mean?) may go on a week-end binge and develop pancreatitis together with elevated triglycerides, but such an episode would be called “alcoholic AP”, not “hypertriglyceridemic AP”. Authors must make sure that there were no patients with alcoholic pancreatitis in their series, no matter how elevated triglycerides were at admission. The fact that there were many men and few women in these series argues in favour of an alcoholic etiology for HTG. Please, re-evaluate the clinical histories or the own patients to attempt to find out daily grams of alcohol consumed at the time of AP.

2. Many patients were investigated while under fibrate treatment, with ensuing modification of lipoprotein values and LPL activity.

3. Table 1 shows that nearly 50% of patients in both groups were under fibrate treatment? If these patients had chylomicronemia syndrome, how were the remaining 50% treated? Were they receiving marine n-3 fatty acids and at what doses? Else, in the case of the patients with prior AP, had some of them lost so much weight since the AP episode that they were now nearly normolipidemic and did not require treatment? Data on weight changes from admission for AP to present evaluation would be interesting to know.

Minor essential revisions

M & M:
1. HP is not a good acronym. Suggest using HTG with AP and HTG without AP to describe the 2 groups.

2. The methods for biochemical analyses are well described, except lipoprotein separation. Please, describe with more detail (ie, densities for each lipoprotein class).

3. There is no clear description of the study protocol, i.e., the information sought from the patients, measurement of anthropometric variables and adiposity, how was family history of dyslipidemia ascertained: Were all available relatives of each patient screened or the information was based on patients’ recall? What were the diagnoses, i.e, familial hypertriglyceridemia (FHTG), familial combined hyperlipidemia, etc.? FHTG is a likely disorder in patients with chylomicronemia. Which diagnostic criteria were used for the familial lipid disorder? AF is not a good acronym; why not use “Familial hyperlipidemia”? Alcohol consumption is critical, as stated above. A complete list of medications used should be listed. Also, given that Table 1 lists fatty liver as comorbidity, was a liver ultrasound obtained in each patient and only those shown in Table had sonographic criteria for fatty liver? All this should be explained in a paragraph or two dealing with the study protocol.

Results:

4. Review of histories from admission for AP. The lipid profile nearest the episode of AP and the cholesterol and triglyceride values should be shown in Table 2 as “admission lipid values” in medians (interquartile ranges) for those with such data.

5. Table 2. There must be data errors, as chylo cholesterol is too high (chylos contain very little cholesterol compared to Tg) and chylo Tg is higher than total Tg in the AP series (?). One wonders about the precision of the chylo isolation method used (contamination with other lipoprotein fractions?), as data from Figure 1 and statements about chylos being present in 12 fasting samples with Tg below 5.65 mmol/L are puzzling (one does not see 12 points below this level in Figure 1). That values are expressed in mmol/L should be shown in Table 2. As usual, Tg data are skewed (SD higher than mean), thus should be shown as medians (IQ ranges). ApoE genotypes (with all alleles, not only 33 and no33) and the tested apoA5 polymorphism should be shown in this Table (with number preceding percentage).

6. Figure 1. See above for the not obvious 12 data points below 5.65 mmol/L.

7. Table 3. Should be omitted, as it repeats data (with lower numbers) in the first two columns. Explain in text distinguishing clinical features of patients with LPL deficiency.

8. Table 4. Comparisons of lipid/lipoprotein/apolipoprotein values among the 3 groups in this Table have little meaning because all 5 patients with LPL deficiency were untreated while most of the other patients were under fibrate
treatment, which may also increase LPL activity. To be fair, authors should compare lipid values among untreated patients in each group. Why were the LPL deficient patients untreated while having such high triglyceride levels?

9. Figure 2. The order of groups should be the same than in Tables (first HTG with PA).

Discussion:

10. Limitations of the study should be acknowledged. An important limitation is that many patients in both groups were investigated while under treatment with drugs (fibrates, perhaps fish oil) that profoundly affect the outcome measurements of lipid and lipoprotein levels and even LPL activity.

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