Increased Lipid Concentration Is Associated with Increased Hemolysis

To the Editor:
The relationship between serum lipids and erythrocyte membrane fragility is complex (1). As seen in routine laboratory practice, samples with hypertriglyceridemia or mixed hypercholesterolemia and hypertriglyceridemia can present as visibly turbid (“milkshake” appearance), but more often they present as “strawberry milkshake” because of increased hemolysis. The amount of hemolysis appears to increase as the lipid concentration increases, although the extent of this effect is not well characterized.

We investigated whether a relationship exists between an increase in total lipid concentration (cholesterol plus triglycerides) and hemolysis in actual patient samples. To determine this relationship, we assessed all samples collected for lipid analysis during 2003 and 2004. Samples from the hospital emergency department were excluded because such samples have a high incidence of being grossly hemolyzed (2).

As a routine procedure, hyperlipidemic samples with a milkshake appearance and optical turbidity (i.e., it was not possible to see through the sample) were analyzed for cholesterol, triglycerides, and amount of hemolysis [hemolytic index (HI)] on the Hitachi Modular System with Roche reagents (Roche Diagnostics) and the Hitachi Modular System with triglycerides, and amount of sample) were analyzed for cholesterol; Table 1). The mean HI for each group was then determined. For lipemic samples containing triglyceride concentrations >15 mmol/L, HI was evaluated after ultracentrifugation. Lipemia did not affect the HI when the triglyceride concentration was <15 mmol/L, but when the triglyceride concentration was >15 mmol/L, we observed an increase in spectrophotometric artifacts (data not shown).

We used the association between hyperlipidemia and hemolysis [ln(HI)] to normalize results for all samples. Multiple linear regression analysis of ln(HI) values indicated that both cholesterol (P < 0.001) and triglycerides (P < 0.001) were linearly related to the HI. The data at higher lipid concentrations (Table 1) suggest that the triglyceride concentration has a greater influence on the HI than the cholesterol concentration. Interestingly, for paired groups with similar triglyceride concentrations, those with a higher cholesterol concentration had a slightly lower HI. A detailed discussion as to possible mechanisms for this observation is beyond the scope of this letter.

These results demonstrate that increasing hyperlipidemia (particularly hypertriglyceridemia) is associated with increased hemolysis. Whether this association is causal is debatable. It is possible that increased lipid concentrations alter the lipid composition of the erythrocyte membrane, leading to increased erythrocyte fragility, with subsequent leakage of cellular content such as hemoglobin. This erythrocyte fragility may be exacerbated as blood moves through collection needles and gel pores, increasing the ease with which these cells can be lysed, with a resulting increase in hemolysis. Such an association has been noted in patients with inherited metabolic diseases in which hyperlipidemia is related to primary lipoprotein lipase deficiency (3), Tangier disease (4), and lecithin:cholesterol acyltransferase deficiency (5). In experimental systems, erythrocyte membrane fluidity has decreased as cholesterol increases (1, 6, 7).

In summary, hyperlipidemic samples are associated with increased hemolysis, possibly the result of increased erythrocyte membrane fragility induced by alterations in membrane lipid content.

References

Goce Dimeski* Andrew Carter

Departments of 1 Chemical Pathology and 2 Haematology Queensland Health Pathology Service Princess Alexandra Hospital Woolloongabba, Australia

* Address correspondence to this author at: Department of Chemical Pathology, Queensland Health Pathology Service, Princess Alexandra Hospital, Ipswich Road, Woolloongabba, Queensland 4102, Australia. Fax 61-7-3240-7070; e-mail Goce_Dimeski@health.qld.gov.au.

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Table 1. Range of HI observed with increasing total lipid (triglycerides plus cholesterol) concentrations.

<table>
<thead>
<tr>
<th>Triglycerides, mmol/L</th>
<th>Cholesterol, mmol/L</th>
<th>n</th>
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