How Does Bezafibrate Affect the Plasma LDL Cholesterol Levels?

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Bezafibrate is a widely used fibrate with a substantial triglyceride (TG)-reducing effect and high-density lipoprotein cholesterol (HDL-C)-raising effect. However, the effects of this lipid-lowering drug on the plasma LDL-C levels are not as clear as those on the TG or HDL-C levels. The J-BENEFIT (Japan BEzafibrate clinical Effectiveness and Tolerability) study was a prospective observational study comprising 6,407 dyslipidemic subjects with diabetes or hyperglycemia. In that study, there were almost no changes in the LDL-C levels after bezafibrate treatment.

In both the St. Mary's, Ealing, Northwick Park Diabetes Cardiovascular Disease Prevention (SENDCAP) Study and Bezafibrate Infarction Prevention (BIP) study, which were conducted in subjects with an average baseline TG level of 200 mg/dL, there were modest reductions in the LDL-C levels.

In the current issue of J Atheroscler Thromb, the subgroup analysis of J-BENEFIT by Hirose et al. showed that bezafibrate has a different effect on the LDL-C levels depending on the pre-treatment LDL-C or TG level. The higher the pre-treatment level of LDL-C, the greater the reduction of LDL-C produced by bezafibrate. On the other hand, the higher the pre-treatment level of TG, the lower the reduction of LDL-C, or the LDL-C level even increased.

Therefore, we are interested in knowing what happens in terms of the properties of LDL particles in those subjects with increased LDL-C levels after treatment with bezafibrate. Recent studies suggest that the increased LDL level associated with bezafibrate treatment may not necessarily be undesirable because this treatment causes a shift in the LDL subclass distribution toward larger particle species. In addition, our previous findings showed that bezafibrate treatment is associated with an increase in the LDL-C level from 164 to 178 mg/dL in type IIb subjects. A detailed analysis of lipoproteins in that study showed that this change in LDL-C was explained by a 10% decrease in small- to medium-sized LDL cholesterol and a 16% increase in large-sized LDL. Considering the previous findings that small dense LDL is an important predictor of cardiovascular risk, the shift in the LDL particle size during treatment with bezafibrate is highly likely to be beneficial.

The BIP study showed that bezafibrate treatment causes cardiovascular event reductions in subjects with a plasma TG level of >200 mg/dL but not those with a TG level of <200 mg/dL at baseline. The authors presumed that the reduced TG and increased HDL-C levels induced by bezafibrate treatment contributed to this event reduction; however, they did not mention the changes in LDL-C in subjects with a plasma TG level of >200 mg/dL during the treatment. Given the present findings of Hirose et al., it is possible that the LDL-C level was increased during bezafibrate treatment in the high TG subjects in the BIP study, although that study was conducted among subjects with a different race or ethnic background than the J-BENEFIT study. We assume that the changes in the properties of LDL-C instead of the concentration of LDL-C as well as the reduced TG and increased HDL-C levels contributed to the beneficial outcomes in the high TG subjects in the BIP study.

Conflicts of Interest

The author declares that he has no conflicts of interest associated with this manuscript.

References

2) Elkeles RS, Diamond JR, Poulter C, Dhanjil S, Nicolaides AN, Mahmood S, Richmond W, Mather H, Sharp P,
Table 1. Effects of bezafibrate on the plasma LDL-cholesterol levels

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of subjects</th>
<th>Baseline TG mg/dL</th>
<th>Baseline LDL-C mg/dL</th>
<th>LDL-C reduction</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENDCAP</td>
<td>83</td>
<td>P 185</td>
<td>P 153</td>
<td>P + 0.6%</td>
<td>2)</td>
</tr>
<tr>
<td></td>
<td>81</td>
<td>B 198</td>
<td>B 141</td>
<td>B - 9.6%</td>
<td></td>
</tr>
<tr>
<td>BIP</td>
<td>1542</td>
<td>P 145</td>
<td>P 149</td>
<td>P - 1.3 mg/dL</td>
<td>3)</td>
</tr>
<tr>
<td></td>
<td>1548</td>
<td>B 145</td>
<td>B 148</td>
<td>B - 6.5 mg/dL</td>
<td></td>
</tr>
<tr>
<td>J-BENEFIT</td>
<td>3316</td>
<td>332</td>
<td>125 (n=2226)</td>
<td>+ 1.6%</td>
<td>1)</td>
</tr>
</tbody>
</table>

P, placebo; B, bezafibrate
SENDCAP, St. Mary’s, Ealing, Northwick Park Diabetes Cardiovascular Disease Prevention
BIP, Bezafibrate Infarction Prevention