Sir,

I read with interest the editorial comment on the CARE-2 study by Professor Floege [1]. Previous studies on the progression of calcification comparing calcium-containing phosphate binders (CaPBs) and sevelamer found that the use of CaPBs is associated with a faster progression of calcification and suggested the higher ingestion of oral calcium as the cause; yet, the effect of sevelamer as a bile acid sequestrant on LDL cholesterol might have contributed to the study findings [2–4]. The CARE-2 study revealed that the difference in the progression of calcification does no longer exist if serum lipids are kept within the same range in both study groups, regardless of the calcium binder used [5]. LDL control, rather than limiting oral calcium intake, appears to be the major factor in attenuation CAC progression in patients on sevelamer.

The importance of serum cholesterol in the progression of calcification is largely disregarded in Floege’s comment on the study. Instead, his attempts to reconcile the findings of the CARE-2 study with those of previous studies are based on a rather unusual interpretation of the data. He proposes that the higher percentage of smokers and patients with diabetic nephropathy in the CARE-2 study puts this population at higher risk of cardiovascular calcification compared with the TTG population [2], and that this elevated risk overrides the benefit of sevelamer. However, it is important to note that within each study, there were no differences in the risk profile between the treatment groups. If calcium intake did significantly accelerate the progression of calcification, the CaPB group in the CARE-2 study should still experience faster progression of calcification than the sevelamer group that was otherwise exposed to the same high risk.

Floege notes that ‘the numeric difference between the sevelamer and calcium group is almost identical at 37 points in TTG versus 30 points in CARE-2’. However, it is unusual to compare absolute changes without considering the difference between groups as a proportion of total change from baseline, and it appears inappropriate to make direct comparisons of absolute changes. The numeric differences between median absolute changes might have been similar, but because the absolute changes were much smaller in the TTG study, the difference was significant, while it was not significant in the CARE-2 study.

In order to answer the initial question as to whether we should ‘CARE-2 avoid CaPB’: No; instead, we should take care to achieve well-controlled LDL cholesterol, phosphorus, and calcium in our patients.

Conflict of interest statement. None declared.

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Calcium-containing phosphate binders: should we CARE-2 avoid them?

Reply

Sir,

I thank Dr Rottembourg for his comment on my editorial, in which he concludes that I have neglected the issue of LDL cholesterol in the interpretation of both CARE-2 and TTG studies. He also concludes that we should aim for well-controlled LDL cholesterol levels as a means to attenuate progression of vascular calcification in HD patients. In response, we need to have a look at the facts again:

1. All studies investigating risk factors for cardiovascular calcification in HD patients consistently have failed to identify a relationship between serum cholesterol levels and the extent of calcifications.
2. Dr Rottembourg proposes that in the CARE-2 study, LDL control was the major factor in attenuating calcification progression in patients on sevelamer. In the CARE-2 study, almost 80% of the sevelamer patients and 100% of the calcium patients received a statin. Despite this, progression of cardiovascular calcification was much more rapid than that observed in the TTG study. The CARE-2 study lacks a control group that had received no statin. According to Dr Rottembourg’s hypothesis, this group should have exhibited an extremely rapid progression. In the absence of such a treatment group, his conclusion that LDL cholesterol control...