특별강연

Serum Alkaline Phosphatase and other Biomarkers of CKD-MBD: Impact on Patient Outcomes

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Hyperphosphatasemia or hyperphosphatasia refers to disorders that feature elevated serum alkaline phosphatase (ALP) activity in the blood. High serum ALP level in CKD patients is usually from excesses of the bone isoforms of the enzyme, but it may also happen in certain types of liver disorders and biliary obstruction. Whereas serum ALP used to be a traditional measure for the management of kidney bone disease, in recent years it appeared to have fallen out of favor, although it is now reviving. A recent epidemiologic study has shown robust associations between higher serum ALP (esp. if >120 U/L) and poor survival in hemodialysis patients. Indeed, compared to serum PTH, which has a U-shaped association with mortality, serum ALP appears to have a linear and incremental association with both all-cause and cardiovascular mortality and this association appears to hold across different PTH strata including PTH below 150 pg/mL. Since lower ALP is associated with lower PTH (and ultimately with hypOdynamic bone), some might expect a higher, rather than lower, mortality associated with low serum levels. Our epidemiologic findings are contrary to this expectation, suggesting that ALP may be more than a mere marker of bone turnover. Higher ALP has indeed been shown to result in increased hydrolysis of pyrophosphate, which is a potent inhibitor of vascular calcification. The effect of ALP on pyrophosphate could be the link that explains why lower levels of the former are associated with a linear decrease in mortality. Indeed, a recent epidemiologic study found that higher levels of ALP, and no other biomarkers such as PTH or minerals, were associated with coronary artery calcification in hemodialysis patients. Another possible explanation for the observed association is a link between higher alkaline phosphatase levels and lower 25(OH) vitamin D level, which is per se associated with increased mortality. ALP is a marker of bone resorption, and its rise in CKD patients is associated with worsening bone mineral density. ALP can be effectively lowered by both active vitamin D amalogues and calcimimetics. Indeed a recent meta-analysis, which questioned the PTH lowering effect of active vitamin D analogs, showed that these agents can decrease serum ALP effectively. Recent data indicate a link between pyrophosphate and tissue-nonspecific ALP as a causative pathway to vascular calcification. A recent study suggested that the lower serum ALP the better is the response of dialysis patients to erythropoietin stimulating agents during anemia management. The consistency of epidemiologic and experimental data on ALP and the fact that vitamin D and calcimimetics can both lower its circulating level makes this traditional marker a promising tool for the management of *Kidney Bone Disease*, notwithstanding that lack of adequate recommendations by current guidelines.

References

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