Alkaline Phosphatase: The Poor Man's iPTH - An Affordable Approach to Bone Health Assessment

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Abstract

This review delves into relatively less discussed role of alkaline phosphatase (ALP) as an accessible alternative to intact parathyroid hormone (iPTH) in the context of bone health assessment, particularly focussing on its potential boon for underprivileged individuals with chronic kidney disease (CKD) in South Asia. The financial constraints faced by this demographic often hinder regular monitoring of iPTH levels. ALP emerges as a promising surrogate, offering a cost-effective and practical solution for bone health evaluation in resource-constrained settings.

Keywords: PTH, Intact Parathormone, Alkaline Phosphatase, ALP, Chronic Kidney Disease, Bone Health

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Introduction

Navigating the intricacies of bone health assessment becomes particularly challenging for underprivileged individuals grappling with chronic kidney disease (CKD) in South Asia. The financial constraints faced by this vulnerable demographic not only underscore the importance of regular monitoring but also shed light on the hurdles associated with adhering to recommended practices.[1-3] The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines advocate for the routine measurement of intact parathyroid hormone (iPTH) levels in CKD patients, emphasizing its pivotal role in managing CKD-metabolic bone disorders including renal osteodystrophy.[4,5] However, the economic realities in South Asia often hinder the widespread adoption of this recommendation, leaving a crucial gap in the comprehensive care of CKD patients. This introduction sets the stage for examining the potential of alkaline phosphatase (ALP) as a practical and economically viable alternative to iPTH, specifically tailored to address the challenges faced by underprivileged CKD patients. ALP, with its accessibility and affordability, may be used as practical alternative, offering a feasible solution aligned with the KDIGO guidelines for effective bone health management.

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The Quest for a Practical and Economic Marker

In the pursuit of a practical and economically viable marker for assessing bone health among underprivileged individuals with CKD, the challenges associated with adhering to recommended practices, particularly the measurement of iPTH as per the KDIGO guidelines, become increasingly apparent. The financial constraints of this demographic often render routine iPTH (cost in South Asia USD 15 to USD 22) monitoring impractical, creating a significant gap in the holistic management of CKD-metabolic bone disorders. Recognizing this predicament, the focus shifts to ALP as a potential solution (cost USD 1.0 to USD 1.5). ALP, with its accessibility and affordability, stands poised to fill the void left by iPTH, offering a practical alternative tailored to the specific needs and limitations faced by underprivileged CKD patients.

Discrimination of ALP Isoenzymes

ALPs are group of isoenzymes, situated on the external surfaces of cell membranes, where they catalyse the hydrolysis of organic phosphate esters in the extracellular space. Organs such as the placenta, ileal mucosa, kidney, bone, and liver exhibit varying ALP concentrations. The liver and bone collectively contribute to over 80% of serum ALP, with a minor contribution from the intestine.[6-8] ALPs exist in two forms: tissue-specific and tissue-nonspecific. Tissue-specific ALPs exclusively manifest in specific tissues like the colon, placenta, and germinal tissue under physiological conditions. Notably, tissue-nonspecific ALPs, expressed in the kidneys, liver, and bone, hold clinical significance, constituting the predominant circulating fraction in serum.[6]

The methodological foundation for evaluating ALP as a surrogate for iPTH hinges on the ability to discriminate between different ALP isoenzymes. In clinical contexts, distinguishing between these isoenzymes is crucial for accurate interpretation. Elevated ALP levels are commonly associated with liver conditions, such as hepatitis or biliary obstruction, where hepatic ALP is released into the bloodstream. Additionally, bone-specific ALP plays a key

role in bone metabolism, and its elevation is observed in disorders affecting bone turnover, such as Paget's disease or fractures. Recognizing the diverse sources of ALP isoenzymes is essential for clinicians to interpret elevated ALP levels accurately and diagnose the underlying condition.[6-9]

Biological Rationale

Unveiling the biological intricacies, ALP reveals its multifaceted nature with a spectrum of isoenzymes, among which bone-specific ALP takes precedence.[6-8] In the intricate landscape of underprivileged individuals navigating CKD, the focal point shifts to the prominence of bone ALP. Notably, bone ALP stands out as a key player, intricately involved in bone metabolism and mineralisation.[6,7]

Beyond its biochemical role, the pathophysiological parallels between ALP and intact iPTH unfold. ALP, akin to iPTH, serves as a vital marker of the bone-renal axis.[9-11] Both ALP and iPTH play pivotal roles in regulating bone turnover.[10,11] Intact PTH, a chief orchestrator, influences osteoblastic and osteoclastic activity, thus governing bone remodelling. Concurrently, ALP, with its predominant bone isoenzyme, reflects ongoing mineralisation and bone formation. Elevated levels of both markers signify disruption in bone metabolism.[9-11]

Methodological Considerations

It is crucial to scrutinise the methodological considerations that underpin the reliability and applicability of ALP in the clinical context. The accuracy and consistency of ALP measurements hinge on the employed laboratory assays and the standardisation of testing protocols. Given the diverse isoenzymes of ALP, with bone-specific ALP being of primary interest, selecting assays that accurately discriminate between different forms is paramount. Standardisation efforts within and across laboratories become crucial to decrease pre-analytical, analytical, or post-analytical errors and to ensure the reliability of ALP as a surrogate for iPTH.[6,12,13] Since 2020, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) method has been employed as the reference method for measuring ALP, aiming to achieve international standardisation.[14]

Conclusion

In navigating the intricacies of using ALP as a surrogate for iPTH amid the complexities of CKD, this exploration reinforces ALP's potential as a "poor man's PTH"- a cost-effective alternative with significant promise. The methodological considerations and diverse isoenzymes, while posing challenges, underscore ALP's affordability and practicality, particularly crucial in resource-limited settings like India. ALP's ability to mirror bone-regulating functions becomes a beacon of hope in circumstances where routine iPTH monitoring may be financially burdensome.

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