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Comparison of free κ and λ light chain immunoassays and total (bound and free) κ and λ light chain immunoassays

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To the editor:

We read, with interest, the article by Dr. Zamora-Ortiz, *et al. Poor performance of the total kappa/lambda light chain quantification in the diagnosis and follow-up of patients with multiple myeloma* on the comparison of the total serum light chain assay (sLC), SPE and IFx for screening patients with a suspected plasma cell disorder.[1] The authors also mention a new diagnostic test, the serum free light chain assay (Freelite™, The Binding Site, Inc., San Diego, CA) which, at the time of publication, was not available in México. This situation has recently changed and the test can now be ordered in México (AIMSA Laboratorio).

Monoclonal gammopathies arise from uncontrolled proliferation of abnormal clones of plasma cells that leads to overproduction of monoclonal immunoglobulins. The abnormal plasma cells produce intact immunoglobulins, free κ or λ light chains without an associated heavy chain, or both.

We wish to clarify the difference between the measurement of total light chains and the serum free light chain tests (sFLC). The sFLC assays (Freelite™, The Binding Site, Inc., San Diego, CA) use specific, purified polyclonal antibodies to detect kappa and lambda light chains in biologic fluids only when they are not bound to the heavy chains of intact immunoglobulin molecules. Total light chain assays are offered by several manufacturers (Beckman Coulter, Fullerton CA; Roche Diagnostics, Indianapolis IN). These nephelometric assays measure light chains bound to heavy chains plus free light chains and therefore have much higher reference ranges in serum than the sFLC assays (Normal range for total kappa: by Beckman Coulter 6,290-13,500 mg/L; by Roche 1,380-3,750 mg/L; sFLC by Binding Site 3.3-19.4 mg/L;) with very different sensitivities (Sensitivity for total kappa: sFLC by Beckman Coulter 111 mg/L; by Roche 300 mg/L; by Binding Site 0.3 mg/L) and for Lambda (Normal ranges for total lambda: by Beckman Coulter 3,130-7,230 mg/L; by Roche 930-2,420 mg/L; sFLC by Binding Site 5.7-26.3 mg/L) with also very different sensitivities (Sensitivity for total Lambda: by Beckman Coulter 300 mg/L; by Roche 300 mg/L; sFLC by Binding Site 0.4 mg/L).

The clinical value of measuring total light chain concentrations for the diagnosis and monitoring of monoclonal gammopathies is uncertain. A scholarly review from the Mayo Clinic on applications of serum and urine assays for evaluation of monoclonal gammopathies states "the benefits of this procedure are limited, and it is not recommended".[2] Total light chain measurements are not included in the response criteria or guidelines for the management of patients with multiple myeloma or AL amyloidosis.[3-5]

The utility of the sFLC assays for the diagnosis and monitoring of monoclonal gammopathies has been extensively studied by leading hematologists and myeloma thought leaders throughout the world and their use advocated for diagnosis, monitoring,

and prognosis (IMWG Guidelines[5]). In addition, the serum free light chain assays have been incorporated into diagnostic and response guidelines in multiple myeloma and AL amyloidosis.[3-5]

We agree with Zamora-Ortiz, *et al.,* the total light chain quantification shows a poor performance in diagnosis and follow-up of multiple myeloma patients and its use should not be recommended. With the availability of the Freelite assay in Mexico, the ability to more accurately diagnose plasma cell abnormalities will become more routine.

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