Multicenter Evaluation of New Free Light Chain Methods

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Abstract

BACKGROUND: The International Myeloma Working Group has provided consensus guidelines for the use of immunoglobulin free light chain (FLC) determinations in the diagnosis and management of clonal plasma cell disorders. We describe preliminary repeatability, linearity, reference range, and method comparison data for two new immunosassays designed for the detection of free Ig light chains type kappa and lambda in serum and plasma. In addition, we investigated samples from patients with kidney impairment for their FLC content.

METHODS: Latent-enhanced mouse monoclonal antibody reagents from Siemens for free Ig light chain type kappa (N Latex FLC kappa) and free Ig light chain type lambda (N Latex FLC lambda) were assayed on three BN II systems1 and three BN ProSpec systems2 using serum samples. Precision studies were carried out according to CLSI guideline EP15-A2 to estimate repeatability performance of three sample pools and two controls each for kappa and lambda, using up to three independent repeat and calibrator lots at the four test sites. Linearity was calculated by evaluating the recovery of repetitions performed at higher or lower dilutions compared to the results obtained with the default dilution. Reference ranges were conducted using 397 clinical samples from apparently healthy adults (aged 16–89 years). Qualitative method-comparison studies using 314 samples from patients with diagnoses of multiple myeloma, amyloidosis, Waldenstrom’s macroglobulinemia, monoclonal gamopathy of undetermined significance, polyclonal immunoglobulin stimulation, or renal disease were performed at two U.S. sites against commercially available FLC methods for the BN II system. For each sample, the deviation of recovery compared to the results from the initial dilution was calculated and expressed as percent deviation. The obtained results were plotted as box plots and compared.

RESULTS: ANOVA studies for between-site, between-lot, and total precision for kappa on the BN II system were 1.7–2.1%, 2.0–3.1%, and 3.7–5.2%, respectively. On the BN ProSpec system, the corresponding kappa results were 2.6–5.2%, 2.4–4.8%, and 3.6–6.9%. Lambda results on the BN II system were 0.4–3.7%, 3.5–7.8%, and 6.2–9.1%, on the BN ProSpec system, lambda results were 1.8–2.5%, 1.2–5.6%, and 4.3–7.7%. In terms of linearity, there were 78 kappa and 117 lambda data sets available for analysis. For kappa 89% and for lambda 97% of the repeats recovered within ±20% of the initial value. Reference-range studies resulted in k. ratio of 0.19/0.87/1.74 (min/median/max). Method-comparison studies resulted in the following: Site 1 analyzed 139 samples and revealed concordance rates of 89.9% for kappa, 77.0% for lambda, and 91.4% for the k. ratio. The results at Site 2 based on 175 samples were 88.6%, 81.7%, and 89.1%, respectively. Combining the data revealed concordance rates of 89.2%, 79.6%, and 90.1%. N Latex FLC results for 57 patients with kidney impairments ranged from 14.1–208 mg/l for kappa and 15.1–228 mg/l for lambda, respectively, and resulted in a k. ratio distribution of 0.430/0.781/1.461 (min/median/max).

CONCLUSION: The new FLC methods performed well under routine laboratory conditions on both BN platforms.

Introduction

FLC (free light chains) are secreted by immunoglobulin-producing plasma cells. FLC kappa circulates as a monomer of 29 kD, whereas FLC lambda usually is present in dimers of 59 kD. As small proteins, FLC are freely filtered by the kidney, the short half-life time is important for monitoring therapy response in monoclonal light chains. The overall precision performance of both methods on each analyzer and between BN platforms was determined. Reproducibility was estimated during a 10-day evaluation period with three reagent methods from The Binding Site, Ltd. for the method-comparison studies. Both analyzer platforms used pre-reaction software protocols to detect antigen stimulation. A total of three BN ProSpec and three BN II systems were used during the evaluation. For the method comparison, all samples were analyzed using routine laboratory conditions on both BN platforms.

Materials and Methods

Instruments

A total of 397 clinical samples on each method were analyzed in duplicate for between-site, between-lot, and total precision.

Materials

The N Latex FLC reagents consist of individual reagent pools for FLC kappa and FLC lambda. A single calibrator and two levels of controls, each available separately, are included. Random distribution of reagent and control lots across sites was applied. All samples were analyzed with the methods in routine clinical use.

Procedures

Repeatability was estimated during a 10-day evaluation period with three reagent lots combinations using three BN II and three BN ProSpec systems. Three samples and two controls were analyzed in duplicate out of two separate sets twice a day. For each sample, the deviation of recovery compared to the results from the initial dilution was calculated and expressed as percent deviation. The obtained results were plotted as box plots and compared.

Conclusion

The N Latex FLC methods performed well in these studies. According to all evaluation sites, they have the potential to become a valuable tool as an aid in diagnosing and monitoring plasma cell proliferative diseases.

References

1. Siemens Healthcare Diagnostics Products GmbH, Marburg, Germany.
2. Foundation of Blood Research, Sudbury, MA, U.S.
3. Henry Ford Hospital, Detroit, MI, U.S.
4. University of Western Ontario, Windsor, ON, Canada.
5. en.wikipedia.org/wiki/Serum_Free_Light_Chain_Measurement

Figure 1. Results of the reproducibility study.

The overall precision performance of both methods on each analyzer and between analyzers was rated as being acceptable by all sites.