Letter to the Editor

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Automated Mindray CL-1200i chemiluminescent assays of renin and aldosterone for the diagnosis of primary aldosteronism

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To the Editor,

Primary aldosteronism (PA) is the most common, but even the least identified cause of arterial hypertension characterized by low levels of plasma renin and high plasma levels of aldosterone (ALD). The latter are inappropriately high for the volume and blood pressure status [1]. Despite several harmful consequences on the heart, arterial wall, and its common occurrence, PA is rarely diagnosed, mainly because it mimics primary (essential) hypertension, but also for the scarce of availability of accurate and reliable laboratory tests to be performed on automated platforms. In fact, in addition to the measurement of serum ALD, the diagnosis is based on the aldosterone/renin ratio (ARR), which is the ALD concentration divided by plasma renin [2]. Until some years ago, the measurements of both ALD and plasma renin activity (PRA) have been performed by radioimmunoassays which were time consuming, affected by risk of errors related to manual procedures and medico-legal associated problems of radioactive waste.

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In addition, available methods for measuring renin, including both the plasma renin activity assay and the direct active renin concentration (DRC) assays have been found to be inaccurate in the low range of renin values. The same poor analytical sensitivity issues have been reported for ALD assays [3].

More recently, more sensitive chemiluminescent immunoassays for ALD and direct active renin have been developed and automated on high-throughput platforms to provide both accurate and rapid results [4].

Here, we describe the main performances of two novel fully automated competitive binding chemiluminescent assays for ALD and renin automated on Mindray CL-1200i (Shenzhen Mindray Bio-Medical Electronics Co, Shenzhen China), with measurement execution times of 41 min for ALD and 26 min for renin.

Traceability: The traceability process for both assays is based on EN ISO 17511:2003; the measured (analyte) in the calibrators for renin is traceable to WHO Reference Material IPR68/356, while for ALD is traceable to a commercial ALD test (CLIA).

Analytical sensitivity: The ALD (CLIA) reagent kit has an analytical sensitivity of 40.2 pmol/L and a functional sensitivity of 47.9 pmol/L. Renin assay has an analytical sensitivity of 0.84 mIU/L and a functional sensitivity of 1.17 mIU/L. The linearity range for ALD spans from 40.2 to 5,540 pmol/L and for renin from 0.835 to 835 mIU/L.

Imprecision: Imprecision studies performed according to the EP5-A3, demonstrated for ALD a repeatability coefficient of variation (CV%) of 1.95% at 609.9 pmol/L and 1.54% at 4,210.9 pmol/L, respectively. The within-laboratory CV%, at the same concentrations, resulted 2.90 and 2.50%, respectively. For renin, the repeatability (CV %) was found to be 1.71% at 21.3 mIU/L and 1.60% at 87.3 mIU/L, respectively. The within-laboratory CV%, at the same concentrations, resulted 2.28 and 2.23%, respectively.

Correlation studies: The LIAISON® XL [DiaSorin, Saluggia (VC), Italy] analytical system was used for comparability study with respect to Mindray CL-1200i. Considering the Mindray CL-1200i results, correlation

studies have been performed for a total of 243 plasma EDTA specimens for renin and of 177 serum specimens for ALD, collected in a dynamic range from 1.44 to 2,829.6 mIU/L for renin and from 41.2 to 9,940 pmol/L for ALD.

Bland-Altman analyses of ALD and Renin, reported in Figure 1, showed that, overall, the comparison presented a bias of 173.4 pmol/L (95% CI: 142.2–204.6) and of 9.9 mIU/L (95%: 6.2–13.6), respectively. Differently, the slopes and intercepts of Passing-Bablok regression results and their corresponding 95% CI showed that the comparison for ALD presented a constant and proportional bias, whereas for renin there is a proportional bias. In particular, for ALD the slope is 1.74 (95% CI: 1.61–1.88) and intercept is −64.47 (95% CI: −99.42–24.69); for Renin the slope is 1.16, (95% CI: 1.07 to 1.30) and intercept is 0.55 (95% CI: 0.35–1.14).

Considering the ALD/Renin ratio (ARR), the comparison between Mindray CL-1200i vs. Diasorin LIAISON® XL results were analysed by Bland-Altman and Passing-Bablok regression. Both analyses showed an absence of statistically significant bias between assays Figure 2.

Recovery tests: The recovery tests were performed using two pools. The renin concentration in low (L) pool was 8.7 mIU/L and in the high (H) pool 129.7 mIU/L. A series of

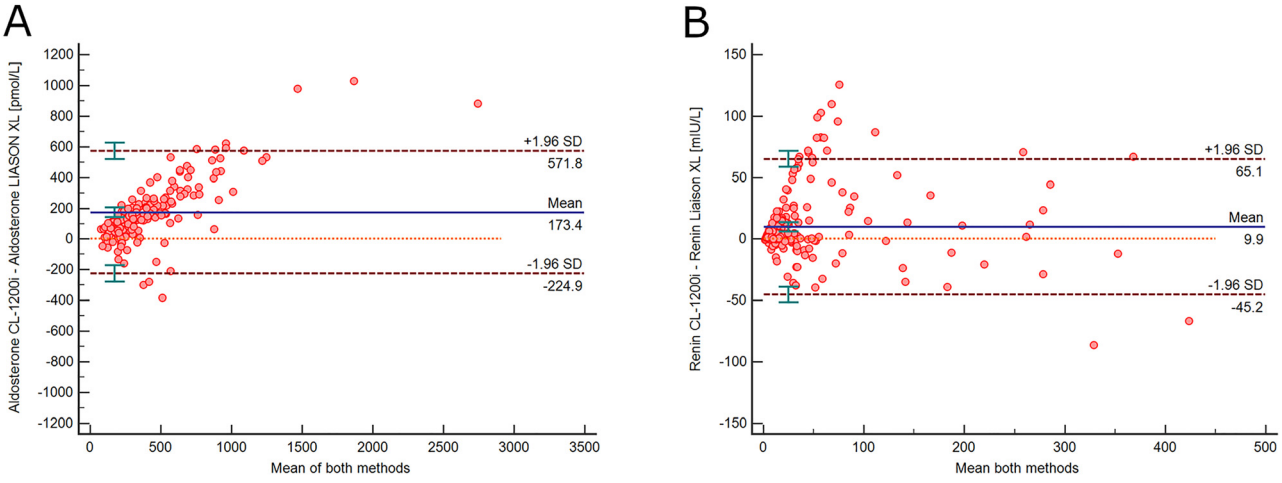

Figure 1: Bland-Altman analyses of Mindray CL-1200i vs. Diasorin LIAISON® XL for aldosterone (A) and renin (B) results. These comparisons were performed using a total of 243 plasma EDTA specimens for renin and of 177 serum specimens for aldosterone, collected in a dynamic range from 1.44 to 2,829.6 mIU/L for renin and from 41.2 to 9,940 pmol/L for aldosterone.

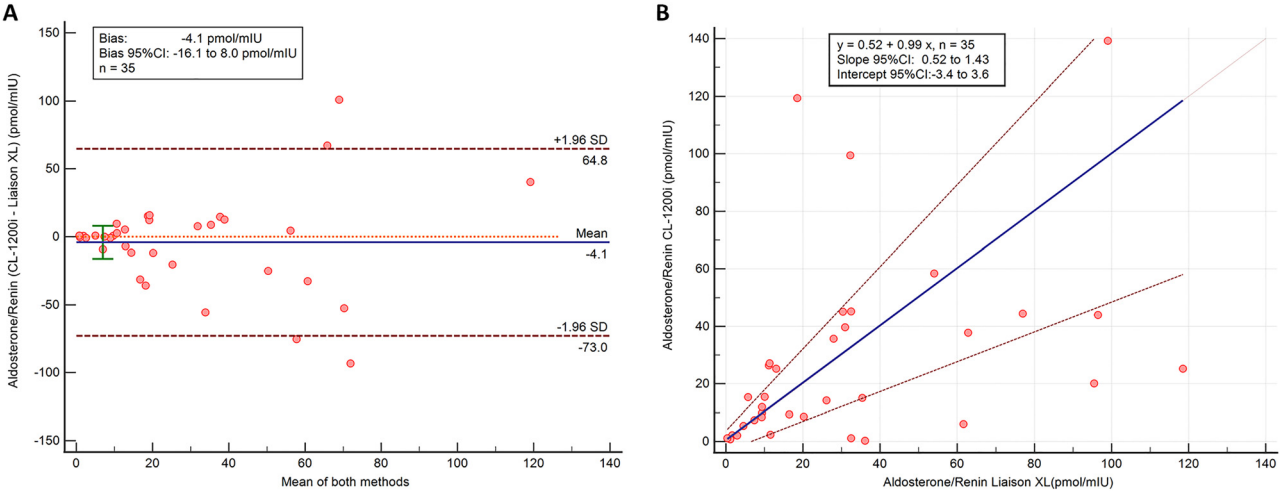

Figure 2: Bland-Altman analysis (A) and Passing-Bablok regression (B) of the aldosterone and renin ratio (aldosterone/renin) for Mindray CL-1200i vs. Diasorin LIAISON® XL.

nine serial dilutions were made by mixing the two pools with the following ratios: 10 (L): 0 (H), 9(L): 1(H), 8(L): 2(H), 7(L): 3(H), 6(L): 4(H), 5(L): 5(H), 4(L): 6(H), 3(L): 7(H), 2(L): 8(H), 1(L): 9(H), 10 (H). The recovery test is show in Supplementary Figure 1. The percentage of recovery ranged from 98.42 to 108.16%. Similar data have been observed for ALD with percentages of recovery ranging from 97.61 to 107.8%.

The data collected highlight the satisfactory analytical sensitivity, imprecision and repeatability of both the Mindray chemiluminescent ALD and Renin assays. In addition, the recovery studies demonstrated a satisfactory accuracy of results within a wide analytical range.

While a bias between the individual assays of Mindray CL-1200i and Diasorin LIAISON® XL for both ALD and renin has been observed, no significant bias has been found for the ARR which assures the most interesting information from a clinical viewpoint, particularly at an appropriate cut-off [1, 4]. However, as a suppressed renin value can increase the ARR even when ALD is normal, to avoid overinflating the ARR value some precaution should be used, particularly in some subgroups of patients who may have low renin values [1].

In conclusion, our data confirm that chemiluminescent assays assure accurate and reliable measurement of both ALD and Renin and that these data, particularly when reported as ARR represents a valuable information for the diagnosis of primary aldosteronism in clinical practice.

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