

FRCPATH Journal Article Appraisal Questions

Question No	Q12	Author	Tetlow
Title	Dorrian CA, Toole, BJ, Alvarez-Madrado S, Kelly A, Connell JMC, Wallace AM. A screening procedure for primary aldosteronism based on the Diasorin Liaison® automated chemiluminescent immunoassay for direct rennin. <i>Ann Clin Biochem</i> 2010; 47 :195-199		
Origination Date	June 2010	Review Date	

	Question	Model Answer
a	Produce a 200 word abstract for this paper, structured under the headings 'Background', 'Methods', Results' and 'Conclusions'	<p><u>Background</u></p> <p>Primary hyperaldosteronism, the most common cause of hypertension, can be screened for using the increase in aldosterone/renin ratio. Diagnostic reliability depends on ability to measure renin at extremely low concentrations. (2)</p> <p><u>Methods</u></p> <p>This paper compares plasma renin measurement by plasma renin activity (PRA) (which is technically demanding and laborious) with plasma renin concentration (PRC) using the Diasorin Liaison (an automated immunoassay). Results from each method were used to calculate the aldosterone/renin ratio (ARR) and performance compared using receiver operating characteristic curves. (3)</p> <p><u>Results</u></p> <p>The analytical and functional sensitivity of the Diasorin method were 2.1 and 5 IU/mL respectively, intra- and inter-assay precision were <7.2% and 10.4% respectively. Significant prorenin interference (9%) was found. Samples with PRA >1.0ng/mL/h showed significant correlation with PRC (r=0.93; P<0.05; n=146) but with PRA <1.0ng/mL/h, no significant correlation occurred (r=0.14; P<0.05; n=79). An aldosterone(pmol/L)/PRC(IU/mL) ratio of >35 in patients with an aldosterone >300pmol/L gave 100% sensitivity and 93% specificity when compared with an aldosterone(pmol/L)/PRA(ng/mL/h) ratio of >750, in identifying patients with potential primary hyperaldosteronism. (5)</p>

		<p><u>Conclusions</u></p> <p>The Diasorin PRC assay is a suitable replacement for the conventional manual PRA assay in calculating ARR as a first line screen for primary hyperaldosteronism. (2)</p> <p>12 marks available</p>
b	<p>Explain why it was important to explore interference from prorenin in the Diasorin assay and outline the method used to do this.</p>	<p>Any prorenin cross-reaction in the renin assay is a significant issue because prorenin concentrations in the peripheral circulation are of the order of 10 times higher than renin. (2)</p> <p>Interference (cross-reactivity) from prorenin was evaluated using a commercial preparation of recombinant prorenin. The recombinant protein was added to seven human plasma samples, containing PRCs within the reference range, to give final prorenin concentrations of 0.5, 5 and 10 ng/mL. Increase in PRC was compared to the amount of exogenous protein added. Duplicate samples were also subjected to trypsin digestion. They were then reanalysed for PRC and the proportion of prorenin measured before and after tryptic digestion compared. (6)</p> <p>8 marks available</p>
c	<p>What is the implication of the recently recognised higher prevalence of this condition on the diagnostic performance of this screening procedure?</p>	<p>The positive predictive value (PPV) of a test improves as prevalence increases.</p> <p>(2)</p> <p>PPV=proportion of patients with a +ve test correctly diagnosed as disease positive. (2)</p> <p>PPV = True Positives/(True positives + False positives)</p> <p>With a prevalence of 1% PPV of the test is 12.5%</p>

		<p>whereas with a prevalence of 10% PPV increases to 62.5%. (4)</p> <p>Negative predictive value (NPV) is proportion of patients with a –ve test correctly diagnosed as disease free.(2)</p> $\text{NPV} = \frac{\text{True Negatives}}{\text{True negatives} + \text{False negatives}}$ <p>NPV is 100% (2)</p> <p>This performance is probably acceptable for a screening test, the purpose of which is to pick up all those who have the disease (in which case false positive rate is less important).(2) Once patients are identified by the ARR screening test, a salt loading test is performed to further investigate the possibility of primary hyperaldosteronism (2)</p> <p>16 marks available</p>
d	<p>Your laboratory currently measures plasma renin activity using a traditional manual radioimmunoassay for anngiotensin I. What are the advantages and disadvantages of replacing this with the Diasorin direct renin assay?</p>	<p><u>Advantages</u></p> <p>Non-isotopic/ more stable reagents (2)</p> <p>Simpler/ less labour intensive (2)</p> <p>Automated/ faster throughput (2)</p> <p><u>Disadvantages</u></p> <p>Sensitivity possibly inadequate. (International guidelines recommend a sensitivity for PRA of <0.3ng/mL/h (equivalent to PRC of 2μIU/mL) although it does not state whether this refers to analytical or functional sensitivity, Analytical sensitivity of the Diasorin assay is 2.1μIU/mL, functional sensitivity is 5μIU/mL) (2)</p>

		<p>New units/cut-offs/reference ranges required (2)</p> <p>Cross-reactivity with prorenin (2)</p> <p>Specific automated platform required (2)</p> <p>14 marks available</p>
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