

Original article

Effect of postural changes on aldosterone to plasma renin ratio in patients with suspected secondary hypertension

Influence de la posture sur le rapport aldostérone sur rénine pratiqué dans le cadre d'une recherche d'hypertension artérielle secondaire

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Abstract

Aims. – To study the influence of postural changes on aldosterone to renin ratio (ARR) in patients with suspected secondary hypertension and to evaluate the sensitivity and specificity of the recommended seated ARR compared to supine and upright ARR for primary aldosteronism screening.

Methods. – Fifty-three hypertensive patients were prospectively hospitalized for secondary hypertension exploration (age: 51 ± 12 , 66% males). After withdrawal of drugs interfering with renin angiotensin system, plasma aldosterone and direct renin concentration were measured in the morning, at bed after an overnight supine position, then out of bed after 1 hour of upright position and finally 2 hours later after 15 minutes of seating. Minimal renin value was set at $5 \mu\text{UI/mL}$.

Results. – Referring to ARR cut-off of $23 \text{ pg}/\mu\text{UI}$, the sensitivity of seated ARR was 57.1% and specificity was 92.3%. The negative and positive predictive values were 95.1% and 45.2% respectively. Compared to these results, a cut-off of 19 improved sensitivity to 85.7% with a specificity of 89.7%. Negative and positive predictive values were 98.3% and 41.1% respectively. Seated ARR mean value was lower than supine and upright ARR mean values, due to an overall increase in renin at seating compared to the supine position by factor 1.9 while aldosterone just slightly increased by factor 1.2. Seated ARR correlated to supine and upright ARR: correlation coefficients (r) 0.90 and 0.93 respectively ($P < 0.001$).

Conclusions. – Current recommended measurement of ARR in the seating position is fairly correlated to supine and upright ARR. A suggested cut-off value of 19 instead of $23 \text{ pg}/\mu\text{UI}$ increased the discriminating power of this test.

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Keywords: Primary aldosteronism; Aldosterone; Renin; Ratio; Secondary hypertension; Sensitivity; Specificity; Supine; Seated

Résumé

Objectifs. – Étudier l'influence des modifications posturales sur la mesure du ratio aldostérone sur rénine (RAR) chez des patients suspects d'hypertension artérielle secondaire et évaluer la sensibilité et la spécificité du RAR assis en comparaison avec le RAR couché et debout dans le dépistage de l'hyperaldostéronisme primaire.

Patients et méthodes. – Cinquante-trois patients hospitalisés de manière prospective pour bilan d'hypertension artérielle secondaire (âge: 51 ± 12 ans, 66 % d'hommes), bénéficient après sevrage conventionnel médicamenteux d'une mesure d'aldostérone et de concentration plasmatique de rénine, le matin couchés, après 1 heure d'orthostatisme et en fin de matinée après 15 minutes assis. Une valeur de rénine $< 5 \mu\text{UI/mL}$.

Résultats. – En se référant au seuil de $23 \text{ pg}/\mu\text{UI}$, la sensibilité du RAR assis atteint 57,1 % et sa spécificité 92,3 %. Les valeurs prédictives négatives et positives sont respectivement de 95,1 % et 45,2 %. En comparaison avec ces résultats, un seuil à 19 améliore la sensibilité à 85,7 % avec une spécificité à 89,7 %. Les valeurs prédictives négatives et positives sont à 98,3 % et 41,1 % respectivement. La valeur moyenne du RAR assis est inférieure à celle des RAR couché et debout, s'expliquant par une moyenne de rénine qui augmente par un facteur 1,9 de la position couchée à la position assise, alors que l'aldostérone n'augmente que par un facteur 1,2. Le RAR assis est bien corrélé au RAR couché et RAR debout: coefficient de corrélation (r) à 0,90 et 0,93 respectivement ($p < 0,001$).

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Conclusions. – Le RAR assis, actuellement recommandé, est bien corrélé au RAR couché et debout. Un seuil suggéré à 19 au lieu de 23 pg/ μ UI améliore les performances de ce test de dépistage.

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Mots clés : Hyperaldostéronisme primaire ; Aldostérone ; Rénine ; Rapport ; Assis ; Couché ; Hypertension secondaire ; Sensibilité ; Spécificité

1. Introduction

Primary aldosteronism (PA) is one of the commonest causes of endocrine hypertension (HTN). Epidemiological studies report different prevalence values of PA in the hypertensive populations ranging from 4 to 10% [1,2]. Independently of HTN, PA could lead to myocardial and renal complications [3,4]. Several studies confirmed the health benefit of screening and specific management of PA. Patients with PA usually present hypokalemia associated hypertension, however, this association has a low specificity and could not be considered as a valuable screening test [5]. Although the association of low renin and high aldosterone profile is the rule in patient with PA, an isolated dosage of direct renin concentration or plasma aldosterone concentration is not a reliable tool to confirm PA owing to high positional or nyctemeral induced variability of these hormones [6]. Many studies confirmed that aldosterone to renin ratio (ARR) is fairly constant on many physiological conditions [6–8], and is considered today as the most reliable tool to screen PA. The adoption of ARR as the screening test for PA led to increased number of PA cases detections [9]. However, this test has its limitations as a diagnostic tool, and should be conducted under well-defined conditions: withholding of all drugs interacting with renin-angiotensin system (RAS), in normal kalemia state and normal dietary sodium intake. If positive, ARR should be corroborated by a confirmatory test (Captopril Test, Fludrocortisone Test or Salt Loading Challenge Test) [10]. Endocrine society and more recently French endocrine and hypertension societies guidelines suggested to measure ARR in the morning after patients have been out of bed for at least 2 h, usually after they have been seated for 5–15 min [10,11]. French societies proposed a cut-off of 23 pg/ μ UI (64 pmol/ μ UI) for diagnosis of PA, which corresponds to the ARR cut-off used in our hypertension centre and used by other HTN expert centres [12,13]. However, we traditionally measured ARR in standardized conditions, with samples collected in the morning, at bed after an overnight supine position [13]. In the study of Tiu et al., the authors assessed receiver-operating-characteristics (ROC) curves, the cut-off values, and the test performance characteristics of ARR in different positions and reported the supine position as the one that offered the best sensitivity and specificity for ARR [8]. However, because it is relatively inconvenient to perform and requiring overnight admission, supine ARR is today replaced by seated ARR that is considered as a more economic screening tool. In order to align with current guidelines, we compared in a population of prospectively hospitalized patients the values of newly recommended seated ARR to traditionally measured supine ARR. We also compared these values to those of upright ARR.

2. Material and methods

Between May 2014 and February 2015, 53 patients were prospectively hospitalized and checked for secondary hypertension in the department of Internal Medicine and Hypertension. As shown in Table 1, included patients fulfilled the criteria defining the persons to screen for PA as announced in the Endocrine Society guidelines: onset of hypertension before the age of 30, hypokalemia associated hypertension (plasma potassium < 3,5 mM) whether spontaneous or under diuretic medications, severe HTN (grade III, with systolic blood pressure [SBP] > 180 mmHg and/or diastolic blood pressure [DBP] > 110 mmHg), resistant HTN as defined by AHA criteria, incidentaloma associated HTN or hypokalemia, and HTN associated with cardiovascular complications [10,14] (Table 1 lists different causes of hospitalization in the studied population). For each patient, we collected anthropomorphic and lifestyle variables: height, weight, body mass index (BMI), cardiovascular risk factors including smoking, usual diet including factors inducing resistance to anti-hypertensive treatments, duration of hypertension, number and classes of anti-hypertensive drugs. SBP/DBP and mean blood pressure were measured by 24-hour ambulatory blood pressure monitoring and/or automatized blood pressure monitoring during hospitalization with validated sphygmomanometer.

3. Biochemical determinations

Biological samples were collected: electrolyte concentrations (sodium and potassium levels before testing); urinary electrolyte analysis in 24 hours collected urines (24 hours urinary potassium and sodium), Plasma RAS hormones concentrations were checked: plasma aldosterone concentration (PAC) was measured by Diasorin Liaison 8600 Radioimmunoassay (RIA) (Normal range 40–175 pg/ml), direct renin concentration (DRC) by ISYS-IDS- chemiluminescent immunoassay

Table 1
Different causes of hospitalization in the enrolled population.

Hospitalisation causes	Number of patients (n = 53)
Hypokalemic hypertension	9
Resistant hypertension (AHA criteria)	21
Severe hypertension	3
Cardiovascular events	1
Adrenal incidentaloma	5
Young age hypertension	9
Not specified cause	5

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