The Endocrine Society's
90th Annual Meeting

Filename: 852181

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Member ID #: 231788 RA

Professional Role: Clinical Researcher

Abstract Format and Category
Session Type: Regular Abstract Session
Presentation Type: Consider for Oral Presentation
Category: 20. Renin-Angiotensin-Aldosterone System/Hypertension - Clinical

Keyword 1: Aldosterone
Keyword 2: Adrenal
Keyword 3: Cardiovascular disease

Awards: None

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Title: HIGH THROUGHPUT ASSAY OF RENIN MASS: INVALUABLE IN THE DETECTION, TREATMENT-TITRATION OR CURE OF LOW-RENIN PATIENTS WITH SALT-DEPENDENT HYPERTENSION

Morris J Brown[1], Susan J Hood[1], Diane E Picton[1] and Kevin P Taylor[2]. [1]Clinical Pharmacology, University of Cambridge, Cambridge, Cambs, United Kingdom, CB2 2QQ and [2]Clinical Biochemistry, Addenbrookes Hospital, Cambridge, Cambs, United Kingdom, CB2 2QQ.

Automated assay of renin mass now permits its routine use in hypertension. We recently reported that in a cohort of patients with elevated aldo(sterone)-renin ratio, plasma renin is more useful than aldo in predicting response to K^+-sparing diuretics or the presence of a Conn's adenoma. In a crossover comparison of diuretics in the cohort, high-dose thiazide was as effective at lowering BP as spiro(nolactone) or amil(oride), but only half as effective in 'de-suppressing' plasma renin (1). We therefore hypothesized that in hypertension, amil is the more effective natriuretic, and that amil + thiazide would cause even greater rise in renin, and BP reduction, than higher doses of either drug alone. The hypothesis was tested in young, low-renin Caucasians. This is a select group, ~5% of young patients, who may be more likely to have discrete causes of Na^+-dependent hypertension than older patients. 30 patients, aged <45, with plasma renin <12 mU/L (≅0.65 ng/ml/hr) rotated in random order between spiro 100 mg, amil 40 mg, bendroflumethiazide (bfz) 5 mg, combo (= bfz 2.5 mg + amiloride 20 mg), frusemide 40 mg and placebo, each taken once daily for 5 weeks. The endpoints were home systolic BP (12 readings over 3 days), and plasma renin. The mean results showed that BP on combo (despite half-doses) was much lower than on either drug alone.

PLASMA RENIN AS MEASURE OF DIURETIC EFFICACY

DRUG	NA	K	CREATININE	RENIN	ALDO (pmol/L)	SBP (mmHg)	DBP
PLACEBO	141	4.0	76.5	8.4	365	138.4	90.4
SPIRO	138	4.4	84.4	42.7	890	132.1	86.7
AMILORIDE	139	4.5	83.6	39.8	1159	130.5	86.2
BFZ	139	3.6	81.6	22.4	435	132.0	85.4
COMBO	138	4.3	84.3	47.1	1147	127.9	85.2
FRUSEMIDE	141	3.8	81.2	15.0	814	133.9	87.4

We confirmed that plasma renin rises twice as much on K^+-sparing diuretics than on thiazide or frusemide, with further increase on combo. Unexpectedly, a Conn's adenoma was found in three patients, despite normal K^+ and aldo at baseline, who dropped their serum K^+ by 1mmol/L on bfz. Post-hoc analysis showed these 3 patients to differ from others in having a suppressed plasma renin throughout the rotation. One patient, with poor BP control throughout, was treated pre-operatively with spiro 25 mg + amil 10 mg. This elevated renin to 138 mU/L and

reduced BP to 124/76 mmHg. We conclude that measurement of renin is invaluable not only in diagnosing patients who require atypical diuretics, but thereafter in titration of treatment so that the need for further investigations and/or diuretic combinations can be recognised.

References: (1) Hood SJ et al. Circulation 2007;116: 268-275

Sources of Support: British Heart Foundation Programme Grant

Author: Susan J Hood

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Author: Diane E Picton

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Author: Morris J Brown

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Author: Kevin P Taylor

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