

# Aldosterone and pressor responses to angiotensin II in primary hyperparathyroidism

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The aim of this study was to assess the effect of hypercalcaemia due to primary hyperparathyroidism on the pressor and aldosterone responses to angiotensin II (Ang II) infusion. Five patients with hyperparathyroidism were studied, before and after parathyroidectomy, and were compared with five normal subjects. After 30 min of equilibration, Asp<sup>1</sup>-Val<sup>5</sup> Ang II was infused in all subjects at stepwise increasing dose rates of 2 and 4 ng/kg per min for 30 min each. In the hyperparathyroid patients the baseline levels of plasma parathyroid hormone and calcium were significantly higher than in the controls, and returned to normal after the parathyroidectomy; plasma aldosterone and renin activity were normal both before and after the parathyroidectomy. Two hyperparathyroid patients had high blood pressure levels, which were normalized after surgery. The increase in the aldosterone response from baseline at each time point of the Ang II infusion was greater in the hyperparathyroid patients before than after the operation ( $P < 0.05$ ), and greater than in the normals ( $P < 0.05$ ). No difference in the increased response of systolic or diastolic blood pressure was observed between the hyperparathyroid patients, either before or after the parathyroidectomy, and the normal subjects. High levels of extracellular calcium or parathyroid hormone, or both, might play a primary role in the aldosterone hyper-responsiveness to Ang II in the hyperparathyroid patients. The similar pressor response to Ang II in hyperparathyroid patients and the normal subjects suggests that hypercalcaemia does not potentiate the vasoconstrictive action of Ang II.

**Keywords:** Angiotensin II infusion, aldosterone, blood pressure, primary hyperparathyroidism.

## Introduction

In primary hyperparathyroidism, hypercalcaemia might have a direct vasoconstrictive action [1] or might mediate the release or the effect of vasoactive hormones [2], or both. The present study was designed to assess the effect of primary hyperparathyroidism on the pressor and aldosterone responses to Ang II infusion.

## Materials and methods

We studied five patients (four females, one male; aged 31-60 years) with primary hyperparathyroidism, before and after a parathyroidectomy, and compared them with five normal age- and sex-matched subjects. Two patients had mildly elevated blood pressure levels, which were normalized within 4 weeks of the operation. No subject was taking any drug and had followed a diet containing 120-150 mmol sodium, 60-80 mmol potassium and 20-30 mmol calcium daily for 2 weeks before the study. Infusion tests were performed when the patients were hypercalcaemic and 6-8 weeks after normalization of plasma calcium due to parathyroidectomy. After 30 min of equilibration in the supine position, Asp<sup>1</sup>-Val<sup>5</sup>-Ang II (Hypertensin, Ciba) was infused, at 0900 h, in all patients at stepwise increasing dose rates of 2 and 4 ng/kg per min for 30 min each. Blood samples were drawn after 0, 15, 30, 45 and 60 min to determine plasma aldosterone. Baseline levels of plasma calcium, phosphorus, sodium, potassium, renin activity, cortisol and parathyroid hormone were also measured. Blood pressure and the heart rate were recorded by an automated sphygmomanometer (Dinamap 845) at 2-min intervals for the duration of the infusion.

Calcium was measured by atomic absorption spectrophotometry, and phosphorus by a colorimetric method. Sodium and potassium were measured by flame photometry. Plasma aldosterone, cortisol and parathyroid hormone 44-68 were measured by radio-immunoassay with kits purchased from Sorin (Italy), Diagnostic Products (USA), and Immuno Nuclear (USA), respectively. Plasma renin activity was measured by radio-immunoassay by the method of Stockigt *et al.* [3].

Basal levels of all parameters, and the increases in aldosterone and blood pressure from baseline at each time point during the Ang II infusion were compared between study groups. Statistical comparisons were made by Student's paired or unpaired t-test, as appropriate. Results are expressed as means  $\pm$  s.e.m.  $P < 0.05$  was taken as significant.

## Results

Abnormally high plasma calcium and parathyroid hormone levels were normalized after surgery, and plasma phosphorus increased slightly. A decrease in blood pressure was observed after surgery, due to normalization in the two hypertensive patients. Plasma sodium, potassium, renin activity, aldosterone and cortisol levels were normal either before or after surgery. Figure 1 shows the mean increases

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plasma aldosterone and diastolic blood pressure over the baseline value during the AngII infusion in the three groups of subjects. The increase in aldosterone was significantly greater for each time point of the infusion in the hyperparathyroid patients before operation compared with the same patients after surgery ( $P < 0.05$ ) or with the normal controls ( $P < 0.05$ ). No difference in the diastolic blood pressure response was observed between hyperparathyroid patients, either before or after the operation, and the normal subjects.

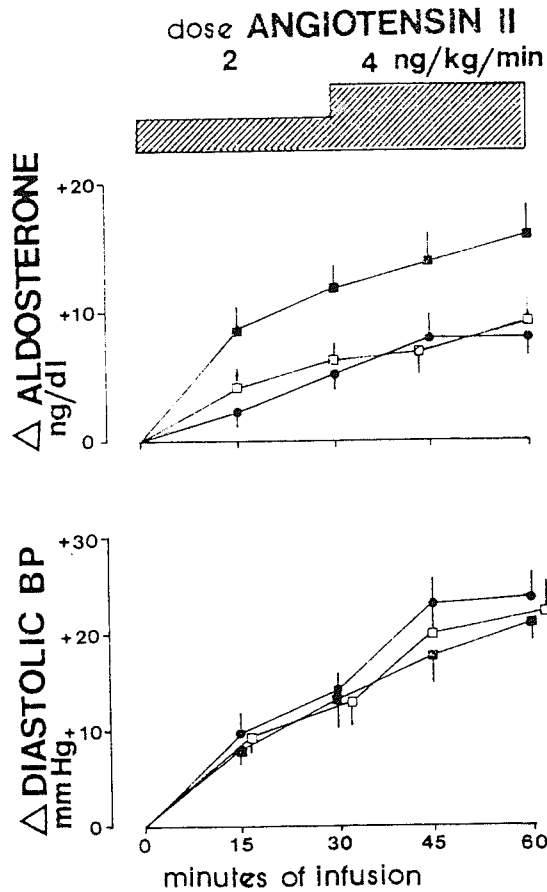


Fig. 1. Mean ( $\pm$  s.e.m.) changes in plasma aldosterone and diastolic blood pressure (BP) levels during the infusion of angiotensin II in normal subjects ( $\bullet$ ) and in hyperparathyroid patients before ( $\blacksquare$ ) and after ( $\square$ ) parathyroidectomy.

### Discussion

The role of calcium in modulating the aldosterone response to angiotensin has previously been studied in humans by testing aldosterone secretion during an infusion of exogenous AngII at different calcaemic levels. Brickmann *et al.* [4] showed that the aldosterone response

to AngII is markedly reduced in patients with chronic hypocalcaemia due to primary hypoparathyroidism. The abnormally enhanced responsiveness to AngII in our hyperparathyroid patients, which was normalized after their return to eucalcaemia, appear to complement these data. In contrast, Bianchetti *et al.* [5] reported no difference in the aldosterone response to angiotensin during hypercalcaemia induced by intravenous calcium infusion, compared with the eucalcaemic state. The reason for the different results may be methodological, i.e. acute versus chronic elevation of calcium levels or non-comparable rates of angiotensin infusion, or may be due to different circulating parathyroid hormone levels. In fact, *in vitro*, a permissive effect has been shown for the parathyroid hormone on calcium-stimulated aldosterone secretion [6]. If this phenomenon takes place *in vivo*, higher levels of parathyroid hormone in our patients compared with presumably low levels of parathyroid hormone in patients given a calcium infusion could explain the enhanced aldosterone response to angiotensin. Our study also demonstrates that the pressor response to AngII is normal in patients with primary hyperparathyroidism, indicating that hypercalcaemia does not potentiate the vasoconstrictive action of this substance. The parathyroid hormone has a direct vasodilator effect, which is at least partly produced by antagonizing the pressor action of naturally vasoconstrictor agents, such as noradrenaline or angiotensin [7]. The normal pressor response to the Ang II infusion seen in our patients might be due to the preventive effect induced by high parathyroid hormone levels.

### References

1. Massry SG, Iseki K, Campese VM: Serum calcium, parathyroid hormone, and blood pressure. *Am J Nephrol* 1986, **6** (suppl 19):19-28.
2. Richards AM, Espiner EA, Nicholls MG, Ikram H, Hamilton EJ, Maslowski AM: Hormone, calcium and blood pressure relationships in primary hyperparathyroidism. *J Hypertension* 1988, **6**:747-752.
3. Stockigt JR, Collins RD, Biglieri EG: Determination of plasma renin concentration by angiotensin I immunoassay: diagnostic import of a precise measurement of subnormal renin in hyperaldosteronism. *Circ Res* 1971, **28** (suppl II):II75-II87.
4. Brickmann AS, Trujillo AL, Gutin MS, Tuck ML: Diminished aldosterone responses to angiotensin II and adrenocorticotropin in hypocalcemic subjects: restoration of responsiveness with normocalcemia. *J Clin Endocrinol Metab* 1987, **64**:297-303.
5. Bianchetti MG, Beretta-Piccoli C, Weidmann P, Boehringer K, Link L, Morton JJ: Studies on aldosterone responsiveness to angiotensin II during clinical variations in calcium metabolism in normal man. *Clin Sci* 1982, **63**:325-328.
6. Olgaard K, Daugaard H, Egljford M: Parathyroid hormone enhances the stimulatory effect of Ca on aldosterone secretion. *Kidney Int* 1986, **29**:168 (abstract).
7. Saglikes Y, Massry SG, Isaki K, Nadler JL, Campese VM: Effect of PTH on blood pressure and response to vasoconstrictor agonist. *Am J Physiol* 1985, **248**:F674-F681.

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