COVID-19 and late-onset hypertension with hyporeninaemic hypoaldosteronism

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TO THE EDITOR:

We have observed hypernatraemia and hypokalaemia with normal serum urea and creatinine associated with new-onset hypertension among COVID-19 patients. We assessed the renin-angiotensin-aldosterone system (RAAS) of 2 patients during the pandemic and found elevated urinary potassium (without causal medications) and hyporeninaemic hypoaldosteronism in both.

We fully investigated a fit 74-year-old woman with COVID-19 who developed hypertension (peak blood pressure (BP) 195/120 mmHg), hypokalaemia (range 2.7–3.2 mmol/L) and hypernatraemia (range 150-166 mmol/L) during the first week of admission. There was metabolic alkalosis with pH 7.50, bicarbonate 31mmol/L, partial pressure of carbon dioxide 5.3 kPa. Adjusted calcium and serum magnesium were normal.

Urinary potassium (K+) was 19.72 mmol/L and 24.46 mmol/L (0-10) on 2 occasions. Plasma renin was <0.2 nmol/L/hr (0.5-3.5) and aldosterone <60 pmol/L (60-250).

Congenital forms of hypertension, glucocorticoid resistance and syndrome of apparent mineralocorticoid excess were excluded. There were no features of hypothalamic-pituitary dysfunction.

She was treated with amiloride 5mg daily increased to 7.5mg after 3 days with normalisation of serum/urinary K+ and BP within 1 week (Table). After 3 weeks amiloride was withdrawn and she remained normotensive. Plasma renin and aldosterone levels remained normal thereafter.

Transient hyporeninaemic hypoaldosteronism may be related to dysregulated sodium (Na+) channel (ENaC) pathophysiology similar to that in Liddle's syndrome. Enhanced ENaC activity (highly selective for Na+ over K+) leads to Na+ retention in the distal nephron and K+ and hydrogen ion secretion to maintain tubular neutrality. This results in intravascular volume expansion and hypokalaemic metabolic alkalosis. This hypothesis is supported by reversibility of electrolyte abnormalities and hypertension with the diuretic amiloride which inhibits Na+ reabsorption by selectively blocking this channel [1,2].

Normalisation of the RAAS during convalescence favour an immediate, self-limiting pathological response related to COVID-19 with a direct effect on ENaC homeostasis leading to a distal tubulopathy.

Viral- angiotensin converting enzyme 2 (ACE2) binding and its degradation in COVID-19 may provide the mechanism. Chen et al. reported high prevalence of hypokalaemia which was difficult to correct because of ongoing renal loss arising from ACE2 degradation. They suggested that reduced counteractivity of ACE2 against ACE1 resulted in disordered RAAS activity and that the end of renal loss of K+ reflected the end of disruption on the RAAS [3]. Our findings support this.

Viral-ACE2 binding may promote Na+ resorption and hypertension via 2 distinct mechanisms which both enhance ENaC activity. Firstly, through increased angiotensin II (AngII) which directly stimulates ENaC activity [7]. ACE2 is abundant in renal tubular epithelium and its downregulation through viral binding increases AngII which in turn increases ENaC activity. And secondly, through increased aldosterone expression. Expression of ACE2 is the principal counter-regulatory mechanism of the RAAS and its downregulation amplifies the ACE-AngII pathway which stimulates aldosterone secretion and augments ENaC activity [4]. Both processes result in Na+ resorption with hypertension and distal tubulopathy with K+ secretion. The first "aldosterone-independent" process is the probable underlying mechanism here and hyporeninaemic hypoaldosteronism reflects appropriate RAAS suppression in response to hypertension and hypokalaemia.

Clinicians should consider investigating the RAAS when faced with unexplained hypokalaemia and hypernatraemia in COVID-19 patients who develop severe hypertension and these patients could be trialled with amiloride.

Legend to Table

Table showing biochemical and blood pressure response to amiloride

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