ON THE PATHOGENESIS OF SECONDARY HYPERALDOSTERONISM WITH ADVANCED CHRONIC RESPIRATORY FAILURE

H. Tzekov

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The increased mineralcorticoid and suppressed glucocorticoid adrenal function established with chronic respiratory failure (CRF) presents an interest, indeed. Some authors report a secondary hyperaldosteronism with CRF without indication of the pathogenetic mechanism (1,3—5,8, 14). V. H. James et al. (1978) explain the lack of arterial hypertension in these patients with the probably reduced angiotensin-converting enzyme (ACE) level or with the production from angiotensin II (AGT II) of larger angiotensin III (AGT III) amounts. AGT III possesses a weaker pressor effect but an equal stimulatory one on aldosterone secretion.

A decreased ACE activity is found out in advanced CRF and respiratory distress syndrome (6,10). High ACE levels are reported in sarcoidosis, farmer’s lung, and histoplasmosis (7,12, 15, 16). Aldosterone secretion regulation is influenced by a series of humoral factors — sodium, potassium, blood volume, etc. Hyperaldosteronuria persists after compensation in patients with right heart insufficiency that argues for the presence of some other factors which influence upon aldosterone secretion along with reduced blood volume in the arterial sector and renal ischemia (5).

The purposes of the present work are as follows:
1. To follow-up plasma renin activity (PRA) changes, ACE, and plasma aldosterone (PA) ones in advanced CRF patients.
2. To try to find a correlation dependence between aldosterone secretion, ACE and disturbed gas exchange.

Material and methods

Our study covered 16 patients (13 males and 3 females) with chronic obstructive lung disease (COLD) — bronchitis form with hypoxemia, pO₂ over 70 mm Hg (9.31 kPa) and hypercapnia, pCO₂ over 49 mm Hg (6.52 kPa). Mean arterial pressure (diastolic+1/3 pulse pressure), pulse frequency, serum sodium and potassium levels and acid-base profile was determined in any patients at a lying position. PRA was determined at basal conditions (after 10-hours patient’s rest at a lying body position). Investigations were carried out without any preceding diuretics and dietary regimen administration. An attention was paid to the circumstance that patients did not receive potassium-saving diuretics during the preceding last 6 weeks. PRA was expressed by AGT I level in ng/ml/h after a radiological method of the firm CEA Sorin. PA was determined in pg/ml by using of putties of the same firm. We used as mean normal values these established by S. Zaharieva and V. Ankov (1982) by using the same method at equal
conditions — pH, etc. (2). Plasma ACE was assessed after the method of Cushman and Chenung in Lieberman's modification (13) and then expressed in U/l. Chronic cor pulmonale without manifestations of clinical decompensation could be established in these patients. That was why a diuretic therapy was not included into the therapeutic complex. Investigations were twofold performed — at patients' hospitalization and on the 15th day after the beginning of treatment.

Results and discussion

Mean arterial pressure was in normal ranges before and in the course of patients' treatment (126.3±11.4—127.9±9.4 mm Hg). Both electrolytes Na and K were also with normal levels. At hospitalization there was an expressed hypoxemia and hypercapnia: \( p_{O_2} = 56.9±6.4 \) mm Hg (7.57±0.85 kPa) and \( p_{CO_2} = 63.8±11.4 \) (8.49±1.52 kPa) (see table 1) accompanied with sinus tachycardia (pulse frequency 96.2±7.4). Basal PRA was 5.6±0.7 ng/ml/h, i. e. statistically significantly increased in comparison with the normal rate (p<0.01). After a 15-day treatment an acid-base balance correction set in, \( p_{O_2} \) increased up to 66.1±4.7 (8.79±0.63 kPa) (p<0.05), and \( p_{CO_2} \) decreased down to 43.9±3.3 mm Hg (5.84±0.44 kPa) (p<0.01). PRA remained high after treatment — 5.1 ng/ml/h while PA diminished down to 74.3±15.2 pg/ml (p<0.001). ACE basal levels were statistically reliably reduced — 7.3±2.1 U/l (p<0.05) and reached normal ones — 15.5±4.9 after hypercapnia disappearance.

There was a strong correlation between PA and \( p_{CO_2} \) (r=0.81, p<0.01) which approximated to the functional one. A moderate reverse correlation was found out between PA and \( p_{O_2} \) (r=0.34, p<0.05). A considerable reverse correlation (r=—0.58) was established between \( p_{CO_2} \) and ACE before treatment in the stage of hypercapnia. The treatment with antibiotics, oxygen therapy, respiratory analeptics, and desobstructive drugs (excluding corticosteroids) induced the correction of hypoxemia and hypercapnia wished for between the third and seventh days after treatment. Our patients were with normal pH and base-excess levels near to the norm. That was why the administration of bicarbonate solutions was not required.

Our results showed that an increased aldosterone secretion was accompanied by a decreased ACE concentration. The increased PRA developed without an arterial hypertension because it was most likely the result of reduced ACE activity. The decreased renal blood supply and renal ischemia caused a long-lasting renin activity enhancement. The low ACE activity gave evidence that
increased aldosterone secretion did not result from the formation of larger amounts of AGT III.

We could draw the following conclusions:
1. Aldosterone secretion does not completely depend upon renin-angiotensin system in case of CRF.
2. Hypercapnia exerts a direct stimulatory effect on aldosterone secretion.

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