Hypoaldosteronism without Hyperkalemia*

P. Weidmann, C. Beretta-Piccoli, Z. Glück, G. Keusch, F.C. Reubi, R. De Châtel, and Ch. Cottier
Medizinische Poliklinik, University of Bern, Switzerland


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**Summary.** Selective hypoaldosteronism has almost invariably been described with hyperkalemia as principal manifestation. The prevalence of hypoaldosteronism and its relationship to plasma potassium, sodium, renin activity (PRA), body sodium-volume state and renal function was evaluated prospectively in 100 non-azotemic patients with diabetes mellitus and 46 with renal disease and normal to moderately impaired kidney function. Ninety healthy subjects served as controls and provided normal ranges for PRA and aldosterone (PA) relative to age and/or sodium excretion. Six diabetics (6%) and 2 renal patients (4.5%) had hypoaldosteronism; their plasma creatinine was <1.4 mg/100 ml. Nineteen diabetics (19%) and 13 renal patients (26%) had borderline hypoaldosteronism; 10 of the renal group had a plasma creatinine of 1.4 to 3.9 mg/100 ml. Plasma cortisol was consistently normal. Except for the presence of hyperkalemia in one patient with borderline hypoaldosteronism and azotemia, plasma potassium was also normal. Mean age, blood pressure, plasma cortisol and electrolytes, urinary potassium, blood glucose (diabetics only) and blood volume, exchangeable sodium and renal function were comparable between low, borderline-low or normal PA subgroups with diabetes or kidney

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Selective hypoaldosteronism with otherwise normal adrenal function [1] is a well accepted cause of hyperkalemia in infants [2–4] or adults [5–9]. The electrolyte disturbance is presumably a consequence of impaired potassium secretion in the distal segment of the nephron. It has been speculated that a concomitant reduction in excretory renal function is the necessary prerequisite for the development of hyperkalemia secondary to aldosterone deficiency [10], but this concept has been disputed [11]. Although hyperkalemic hypoaldosteronism in adult patients was very often associated with mild to marked renal failure [6–9], several cases with normal BUN or serum creatinine levels have been described [1, 5, 12–15]. Nevertheless, these metabolic products are both partly dependent on nonrenal factors and normal values do not necessarily exclude a mild reduction in excretory capacity [16]. Moreover, factors other than renal impairment may have enhanced the tendency for hyperkalemia in some patients with hypoaldosteronism [17]. Therefore, while normal circulating aldosterone levels appear to be indispensable for the maintenance of normokalemia in azotemic patients [9, 18], this relationship in the presence of normal kidney function has been less clear.

Except for an isolated case with renal sodium wasting, hyponatremia and a normal plasma potassium concentration [19], the previously reported adult patients with isolated aldosterone deficiency tended to have hyperkalemia. We describe hypoaldosteronism without hyperkalemia in 8 patients with nonazotemic diabetes mellitus or renal disease. This constellation favors a more facultative role of aldosterone as a protective factor against excess potassium retention in non-azotemic man.

**Patients and Methods**

One hundred patients with diabetes mellitus and 46 patients with renal disease were studied. The diabetic patients included 59 females and 41 males, ranging in age from 19 to 76 yr (mean 58±13 (SD) yr); fasting blood glucose levels were increased in each of these patients. The duration of diabetes ranged from 0.5 to 30 yr (mean 9.5±8.2 yr). Thirty patients were treated by diet, 34 by diet and oral hypoglycemic agents and 36 by diet and insulin. The metabolic state was stable at the time of study. Hypertension (diastolic ≥ 90 and/or mean blood pressure > 107mm Hg) was present in 54 patients, diabetic retinopathy in 36, polyneuropathy in 35, nephropathy as evidenced by proteinuria in 21 and macroangiopathy in 16 patients. None of the diabetics showed clinical evidence of heart failure or edema and all had a serum creatinine < 1.4 mg/100 ml.

The patients with renal disease included 20 females and 26 males, ranging in age from 20 to 65 yr (mean 43±13 yr). The diagnosis was chronic glomerulonephritis in 12 patients, chronic pyelonephritis in 13, interstitial nephritis of various etiology in four, nephrosclerosis in eight, bilateral renal arterial stenosis in one case each. The blood pressure was normal in 10 renal patients and 36 had hypertension. None had congestive heart failure or edema. Seventeen patients had a plasma creatinine below 1.4 mg/100 ml; in the remaining 29 it was elevated, ranging from 1.4 to 6.0 mg/100 ml.

In order to avoid either very low or very high sodium intakes, subjects were instructed to ingest a normal diet but without added salt, starting at least five days before the test. Supine and upright (each for one hour) pulse rate, blood pressure and plasma sodium, potassium, creatinine, renin activity (PRA), aldosterone and cortisol concentrations were measured in the remaining 29 it was elevated, ranging from 1.4 to 6.0 mg/100 ml.

Blood pressure was measured using standard cuff and sphygmomanometer. Each blood pressure or pulse rate was the average of three recordings. The mean blood pressure was calculated as the sum of diastolic (disappearance of sounds) and one-third of pulse pressure. Plasma and urinary sodium and potassium concent-