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Sodium and potassium concentrations of red blood cells and plasma in children with nephrotic syndrome, uraemia and pyelonephritis

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The sodium and potassium concentrations of the red blood cells and the plasma in 38 children with pyelonephritis (19 acute, 10 chronic and 9 healed), 5 children with uraemia, and 20 children with nephrotic syndrome were compared with those of control children. The red blood cell sodium concentration was lower in patients with acute pyelonephritis, uraemia, and steroid-treated nephrotic syndrome, and higher in those with chronic pyelonephritis and nephrotic syndrome not treated with steroids. Except in uraemic cases, these alterations were not accompanied by plasma sodium and potassium changes. The results might be explained by pathological Na^+ and K^+ transport processes in the red cell membrane. The possible role of extracellular fluid volume changes, sodium loss and water retention are discussed.

The Na^+ and K^+ composition of the human red blood cells (RBCs) are close to those of other cells, and the RBC is a good model for the study of intracellular electrolytes and membrane transport processes [1, 18, 19]. The Na^+ and K^+ concentration of the RBCs have previously been investigated mainly from the aspect of cardiac glycosides or arterial hypertension [7, 14, 26, 27].

We have studied the Na^+ and K^+ concentrations of the RBCs and plasma in children with pyelonephritis, uraemia and nephrotic syndrome, with a view to establish whether there was a connection between the type of the disease and the electrolyte differences.

Patients and Methods

The RBC and plasma concentrations of Na^+ and K^+ were determined in 63 children with renal diseases and in 16 healthy control children, by the method described by Fortes Mayer and Starkey [5]. All patients were undergoing treatment in our Department; they comprised 19 with acute pyelonephritis, 10 with chronic pyelonephritis, 9 with healed pyelonephritis, 5 with uraemia and 20 with nephrotic syndrome. There was no difference in age distribution between the patients and the controls. Besides the massive pyuria and bacteriuria observed in urine obtained by bladder puncture, the criteria of pyelonephritis were the clinical symptoms and the decrease in renal concentrating capacity. Cases were regarded as chronic if leucocyturia and bacteriuria had persisted for longer than one month in spite of directed antibiotic treatment. In addition, urinary con-

centrating capacity remained depressed and I. V. urography revealed symptoms of chronic pyelonephritis. In 3 of the nephrotic syndrome patients, a moderate degree of clearance reduction was observed; the others did not display azotaemia. During the time of the examination, the nephrotic syndrome patients received uniform doses per weight of lasix, KCl and spironolactone, with prednisolone or chlorambucil treatment when necessary. 21 observations were performed on 15 patients before or without prednisolone treatment, and 23 observations were performed on 17 patients during prednisolone treatment. Moderate hypertension (average 21.5/12 kPa) was observed in 2 of the nephrotic syndrome patients and 3 of the uraemic patients. They participated in methyldopa and prazosine treatment. A pathological acid-base finding was observed in 2 uraemic patients with a moderate degree of compensated metabolic acidosis kept in equilibrium by the administration of 1 g $NaHCO_3$ daily. The serum urea nitrogen level in the uraemic patients was 22—27 mmol/l; one of them underwent haemodialysis treatment.

Results are presented in Tables I and II. Statistical evaluation was performed with Student's t test.

Results

Table I presents RBC and plasma Na^+ and K^+ concentrations in healthy children and in children with acute, chronic or healed pyelonephritis and with uraemia. A significantly lower RBC Na^+ level was observed in acute pyelonephritis, and a significantly higher one in chronic pyelonephritis. The observed electrolyte values for the healed pyelonephritis cases corresponded to those of the controls. In the uraemic patients, higher plasma K^+ and lower RBC Na^+ concentrations were found. Because of the low number of cases, sigfinicance was not calculated.

Table I

Plasma and red blood cell Na^+ and K^+ concentration in healthy children and in children with acute, chronic or healed pyelonephritis and with uraemia

	n	Plasma Na^+ $\bar{x}$	mmol/l SD	Plasma K^+ $\bar{x}$	mmol/l SD	Red blood cells Na^+ $\bar{x}$	mmol/l SD	Red blood cells K^+ $\bar{x}$	mmol/l SD
Healthy children	16	140	±2	4.0	±0.3	6.5	±0.6	94.4	±3.1
Acute pyelonephritis	19	139	±2	4.1	±0.4	4.8	±0.8**	93.6	±3.1
Chronic pyelonephritis	10	140	±2	4.0	±0.5	7.6	±1.0*	96.4	±3.4
Healed pyelonephritis	9	139	±4	4.1	±0.5	6.4	±0.4	96.0	±4.0
Uraemia	5	137	±6	4.6	±0.5	4.9	±1.2	92.5	±3.8

* $p < 0.01$
** $p < 0.001$

Table II lists the results of the nephrotic syndrome patients. Without steroid treatment, the RBC Na^+ concentration was significantly higher, while the plasma Na^+ concentration was significantly lower than the levels of the controls. In response to steroid treatment, the RBC Na^+ level fell to a significantly lower value as compared to the controls, while the plasma Na^+ increased to normal.

TABLE II

Plasma and red blood cell Na^+ and K^+ concentrations in nephrotic syndrome patients

	n	Plasma Na^+ $\bar{x}$	mmol/l SD	K^+ $\bar{x}$	mmol/l SD	Red blood cells Na^+ $\bar{x}$	mmol/l SD	K^+ $\bar{x}$	mmol/l SD
Before or without prednisolone treatment	21	137	±3*	4.2	±0.9	8.1	±1.4**	93.7	±4.7
During prednisolone treatment	23	140	±2	4.0	±0.3	5.1	±1.1**	93.3	±4.2

* $p < 0.01$
** $p < 0.001$

DISCUSSION

The Na^+ and K^+ concentrations of the control RBCs and plasma were in accordance with recent data in the literature [3, 5].

The lower RBC Na^+ concentration observed in acute pyelonephritis was of interest, as in other investigations higher RBC Na^+ levels were found in diseases involving acute inflammation of the airways. The cause of the latter phenomenon is presumably the inhibitory effect of inflammation on the activity of the Na—K pump. Furthermore in chronic pyelonephritis an impaired urinary concentrating mechanism is leading to polyuria and extracellular water loss. The compensatory water efflux from the cells into plasma causes a relative higher Na^+ concentration in RBC. These changes in Na—K pump activity and extracellular fluid volume are possibly corresponding to the alteration of RBC Na^+ level in chronic pyelonephritis. A possible reason for the lower RBC Na^+ level in acute pyelonephritis is that in pyelonephritis PGE synthesis by the kidney is enhanced [23]. PGE probably inhibits tubular Na^+ and water reabsorption. The process acts in the direction of hyponatraemia, which is counteracted by the Na^+ leaving the RBCs. In healed pyelonephritis the RBC Na^+ level is normal.

Both elevated and depressed RBC Na^+ levels have been described in uraemic diseases [4, 11, 24, 25, 28]. The inhibitory effect of uraemic toxins on the function of the Na—K pump is assumed to be the cause of the elevation in RBC Na^+ level [11, 13]. This was disputed by Funder and Wieth [6], who considered the role of acid-base changes. Cumberbatch and Morgan [2] attributed the lower RBC Na^+ level to the decreased permeability of the membranes. As to the RBC electrolyte changes, Sigström [21] distinguished between slowly and rapidly progressing uraemia. Another possible explanation is that in patients with chronic uraemia a renal sodium loss and water retention exist simultaneously, causing a lower level of sodium in the extracellular fluid. This was counteracted by Na^+ efflux into plasma, and water

transport into RBC. In 4 of our 5 uraemic patients, the RBC Na^+ concentration was depressed, while in some cases higher plasma K^+ values were found.

In the patients with nephrotic syndrome, high RBC Na^+ and low plasma Na^+ levels were observed before or without steroid treatment. Similar values were measured after therapy had been stopped. The cause of the low plasma Na^+ level may have been the systemic diuretic treatment. There may be a number of reasons for the increase in the RBC Na^+ concentration. A role is presumably played in this by lasix treatment, which blocks the Na^+, K^+-ATPase activity. We believe that another important causal factor are the hypercholesterinaemia, hyperlipidaemia and hypertriglyceridaemia typical of the nephrotic syndrome. The pathological lipoprotein composition of plasma leads to a change in the lipid composition of the RBC membrane. Accordingly, there is a change in the fluidity of the membrane, which has a substantial influence on the Na^+, K^+-ATPase activity and the part-phenomena of Na^+ and K^+ transport [10,17]. Jackson and Morgan [10] induced an increase in the RBC Na^+ level by the administration of cholesterol in vitro.

In response to steroid treatment, RBC Na^+ concentration fell significantly as compared to the control level. The effects of steroid treatment on the Na^+, K^+-ATPase activity have already been described [9, 20]. The decrease in RBC Na^+ concentration as a result of steroid therapy has been discussed previously in some patients with various diseases [12]. We did not observe any change in the RBC K^+ concentration; the continuous administration of diuretics may have had a part in this. The plasma Na^+ level was found to be lower before or without steroid treatment, and to normalize when steroids were given. As a consequence of the plasma Na^+ increase and RBC Na^+ decrease in response to steroid treatment, it may be assumed that steroid treatment gives rise to the altered position of the extra-intracellular electrolyte equilibrium by enhancement of the activity of the RBC Na—K pump.

The effect of steroid treatment in decreasing the RBC Na^+ concentration may be connected with the beneficial therapeutic action of the steroids. In work on fibroblast cell cultures Mendoza [15] found that the uptake of Na^+ plays an important role in the regulation of cell proliferation. Since it has been demonstrated that virtually all cell membranes possess Na^+, K^+-ATPase activity [1, 19, 20], the steroids inhibit cell proliferation by decreasing the intracellular Na^+. Further studies are needed to investigate the possible role of natriuretic hormone [8, 22] in the altered membrane transport of sodium during the changes of extracellular fluid volume and in nephrotic patients with and without steroid therapy.

We have attempted to classify the nephrotic syndrome patients in accordance with the basic process. They were divided into steroid-sensitive and steroid-resistant cases. No essen-

tial difference was, however, found between the electrolyte values for the two groups, either before or during prednisolone treatment.

Total-body isotope examinations have revealed that there may be appreciable total-body electrolyte differences, even when the plasma electrolyte composition is normal [16]. Our results demonstrate that the Na^+ and K^+ compositions of the RBCs may vary in different ways than those of the plasma in certain renal diseases.

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