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Renal Regulation of Potassium Homeostasis in Calves in the First Week of Life Including the Role of Atrial Natriuretic Peptide

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The experiment was carried out on 10 clinically healthy Polish-Friesian var. Black-and-White cow calves, during the first seven days of postnatal life. The results indicate that renal removal of potassium depends primarily on the quantity reabsorbed in the tubules, whereas clearance of the electrolyte, due to stable levels in the blood plasma, depends on the amount excreted in the urine. With stable tubular reabsorption of potassium, a relatively unchanging amount of excreted potassium was observed in the urine. However, reduced tubular reabsorption caused a significant increase in excretion and clearance of the electrolyte. Changes in the amount of filtered potassium play a minor role in the regulation of excretion. Small changes in the blood plasma potassium concentration observed primarily resulted from changes in glomerular filtration rate and tubular reabsorption, since the concentration of electrolyte in the blood after birth remained within the physiological range. The results of this study suggest that neonate calf' kidneys are sufficiently prepared to regulate kalemia. Atrial natriuretic peptide is not directly involved in the regulation of tubular reabsorption of potassium in calves in the first week of life, although it is highly likely that the peptide is involved in the excretion of potassium in the urine in calves during the first seven days of life.

Key words: Potassium homeostasis, ANP, kidney, calves, neonatal period.

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Potassium is one of the most important components of body fluids and a major cation of the intracellular fluid. Potassium controls the osmotic pressure and volume of intracellular fluid and is necessary to maintain the resting potential of cell membranes.

Potassium imbalance impairs skeletal muscles and heart function. Improper blood plasma concentration of potassium may result from changes in extracellular space (with over-supply or excessive removal of potassium) or in intracellular space (due to potassium transfer from extracellular to intracellular fluid). Hyperkalemia in calves may be caused by kidney failure or by reduced volume of extracellular fluid under severe dehydration or acidosis resulting from diarrhea. Hypokalemia can result from excessive loss of potassium through the digestive tract (diarrhea) or with the urine (metabolic alkalosis), due to reduced forage intake or due to transition of potassium from extracellular fluid into cells (metabolic alkalosis) (SWEENEY 1999).

Renal regulation of potassium balance is a joint result of both the electrolyte concentration in the blood and the action of hormones that regulate renal function. Elevated blood plasma potassium concentration e.g. due to increased supply, suppresses renin and angiotensin II, while reducing the amount of potassium stimulates the activity of both hormones (WANG & GIEBISCH 2009). Stimulated by a low concentration of blood plasma potassium, angiotensin II inhibits the removal of the electrolyte in the distal tubules of nephrons (WANG & GIEBISCH 2009). Also kaliuretic aldosterone activity is observed only at high concentrations of potassium in blood plasma (DUSSOL 2010; PALMER & FRINDT 2000). During dehydration a significant role in the excretion of potassium with the urine is attributed to vasopressin (WANG & GIEBISCH 2009). Atrial natriuretic peptide (ANP), acting antagonistically to the above-mentioned hormones, contributes to the excretion of potassium in the urine (VORMFELDE *et al*. 2009). Kaliuresis may be the result of the direct action of ANP on the distal tubule or indirect inhibition of activity of RAAS and vasopressin (DRATWA 2002).

This study was aimed to assess the ability of calf kidneys to control kalemia during the first week of life and explain the physiological role of atrial natriuretic peptide in this process.

Material and Methods

The experiment was carried out on 10 clinically healthy Polish-Friesian var. Black-and-White cow calves, during the first seven days of postnatal life. The animals were born by cows that had not shown any clinical symptoms of disease. The parturitions were natural, supervised by the farm workers. After completing the necessary treatments and providing colostrum, calves were transported to the animal house of the Department of Animal Physiology and Cytobiology. During the study period, the animals were housed in individual cages under standardized environmental conditions. Calves were fed colostrum and mother's milk (three times a day) in an amount of 6-7 liters per day.

Blood and urine samples were collected daily in accordance with a previously described procedure (DRATWA 2006). The concentration of potassium in blood plasma and urine was determined photometrically (Flapho-4 flame photometer).

In order to assess the kidney's ability to regulate kalemia, the glomerular filtered load of potassium (F_K), the potassium load excreted with urine, as well as potassium reabsorption were calculated according to the following formulas:

$$F_K = P_K \cdot GFR \text{ (mmol/l)}$$

$$TR_K = \frac{F_K - (U_K \cdot V)}{F_K} \cdot 100 \text{ (\%)}$$

$$C_K = \frac{U_K \cdot V}{P_K} \text{ (ml/min)}$$

Where:

F_K – glomerular filtered load of potassium,

P_K – blood plasma potassium concentration (mmol/l),

GFR – glomerular filtration rate (ml/min),

TR_K – tubular reabsorption of potassium,

U_K – urine potassium concentration (mmol/l),

C_K – potassium clearance,

V – minute diuresis (ml/min)

The collected data were standardized for 1 m^2 of body surface area. Mean values and standard deviations were calculated, the significance of differences was estimated and correlation coefficients were determined. Statistical analysis was performed using the package Statistica 6.0 (DRATWA 2006).

Results

In our previous studies, we demonstrated a statistically significant ($P \leq 0.01$) increase in blood plasma ANP during the first seven days of calf life (DRATWA 2006). On the first day of life, the concentration of the hormone was 5.72 pmol/l, while on day 7, the concentration increased to 14.34 pmol/l. The highest blood plasma ANP concentration was recorded on day 6 (16.43 pmol/l).

The lowest mean value of potassium filtered load was observed on the first day of life, $F_K = 0.14$ mmol/min/m^2 (Table 1). A significant ($P \leq 0.01$) increase in this parameter was recorded on the second day of life, which was followed by a stabilization over the remaining days at an average level $F_K = 0.21$ mmol/min/m^2.

Tubular reabsorption (TR_K) of potassium during the first four days of life was high (67.44% on average) and relatively stable (Table 1). This parameter decreased significantly ($P \leq 0.05$) on the fifth day of life, which was followed by stabilization at a level of 37.07% until the end of the experiment. It should be emphasized that tubular excretion of potassium was observed in some calves from the third day.

Potassium clearance (C_K) and its excretion in the urine ($U \cdot V_K$) of calves increased significantly during the first week of life (Table 1). Excretion of K over the first four days increased from 50.10 μmol/min/m^2 (the first day of life) to 98.26 μmol/min/m^2 (the fourth day of life). The changes, however, were not confirmed at a level of $P \leq 0.05$. A statistically significant increase ($P \leq 0.01$) of the electrolyte excretion in the urine was observed on the fifth and sixth days of life. It should be emphasized that there were large differences in the excretion of the electrolyte among individuals.

In the first week of life, statistically significant changes ($P \leq 0.05$) were observed in blood plasma potassium concentration (P_K) ranging from 3.55 to 4.20 mmol/l (Table 1). The lowest concentration of potassium in blood plasma was noted on the second day of life, and the highest on the fifth day after birth. However, blood plasma potassium concentration remained within the range of physiological standards and oscillated around an average of 3.97 mmol/l.

Table 1

Filtered load of potassum (F_K), potassium tubular reabsorption (TR_K), potassium excretion in the urine ($U \cdot V_K$), potassium clearance (C_K), blood plasma potassium concentration (P_K) in calves in the first week of life and significant differences (SD) between values in the following days of life

Specification		Day of life							Significance of differences	
		1	2	3	4	5	6	7	p≤0.01	p≥0.05
F_K	$\bar{x}$ (mmol/min/m^2)	0.14	0.18	0.21	0.20	0.22	0.20	0.21	1→2-7 2→3, 5	2→4, 7
	SD	0.03	0.02	0.02	0.03	0.03	0.02	0.03		
TR_K	$\bar{x}$ (%)	63.86	63.66	72.88	69.38	41.51	29.17	40.52	2→7 3→6, 7 4→7	1→5, 7 2→6 3→5 4→5-6
	SD	19.57	21.98	20.94	15.32	20.93	22.76	17.35		
$U \cdot V_K$	$\bar{x}$ (μmol/min/m^2)	50.10	62.58	80.64	98.26	180.38	193.97	138.79	1→5-7 2→5-7 3→5-6 4→5-6	–
	SD	27.86	36.49	86.26	81.51	92.96	65.97	52.34		
C_K	$\bar{x}$ (ml/min/m^2)	13.17	17.83	19.06	24.44	42.68	48.33	34.80	1→5-7 2→5-7 3→5-6 4→5	3→7 4→6
	SD	7.37	10.81	19.04	21.68	21.33	16.71	13.78		
P_K	$\bar{x}$ (mmol/l)	3.85	3.55	4.07	4.10	4.20	4.03	4.02	1→2, 5 2→3-7	5→6-7
	SD	0.25	0.13	0.35	0.38	0.30	0.32	0.21		

Discussion

In the first week of the calf life, significant changes were observed in the amount of filtered potassium, potassium tubular reabsorption, and in potassium excretion in the urine. The results indicate that renal removal of potassium depends primarily on the quantity reabsorbed in the tubules, whereas clearance of the electrolyte, due to stable levels in the blood plasma, depends on the amount excreted in the urine. With stable potassium tubular reabsorption, a relatively unchanging amount of potassium excreted was observed in the urine. However, reduced tubular reabsorption caused a significant increase in the excretion and clearance of the electrolyte. Changes in the amount of filtered potassium play a minor role in the regulation of excretion.

The changes in potassium reabsorption observed in the presented experiment were consistent with those reported by SKRZYPCZAK (1991) and OŻGO (2009). SKRZYPCZAK (1991) observed relative stability of this parameter at an average level of 64.35% in the first five days of life and a statistically significant reduction to a value of 33.07% on the sixth and seventh day after birth. OŻGO (2009) showed that stabilization of potassium tubular reabsorption takes place in the first four days of life at an average level of 59.75%. In the subsequent days of life, the author noted a significant decrease in reabsorption to 34.94% on the sixth day, and 39.52% on the seventh day. It should be noted that the statistically significant reduction ($P \leq 0.05$) of potassium reabsorption observed in the presented experiment from the fifth to seventh day of life did not influence changes of electrolyte blood plasma concentrations in the calves.

The experiment revealed no correlation between increasing blood plasma concentrations of atrial natriuretic peptide and changes in tubular reabsorption of potassium (correlation coefficient insignificant at $P \leq 0.05$). Perhaps the decrease in K tubular reabsorption observed from the fifth day of life was associated with a "disclosure" of the kaliuretic action of aldosterone, which was confirmed by OŻGO (2009). The author observed a high concentration of aldosterone on the first day of life, 30.62 pmol/l, a reduction on the second and third days to 18.87 and 19.12 pmol/l, respectively, an increase on the fifth day to 28.39 pmol/l, and a decrease again to 21.74 pmol/l observed on the seventh day.

The increase in potassium excretion in the urine observed in this experiment during the first week of life, as well as the previously noted increase in blood plasma ANP concentration with age (DRATWA 2006), but also the highest amount of potassium clearance observed with the highest blood plasma ANP concentration (DRATWA 2006), may imply (despite the lack of statistical significance) that ANP plays a role in regulation of potassium excretion in the urine. The increase in excretion of potassium in the urine after administration of exogenous ANP to animals, observed in adult dogs (KIMURA *et al.* 1986), adult rats (RAKOTONDRAZAFY *et al.* 1996), and in sheep fetuses (SHINE *et al.* 1987), may confirm the above assumptions. Moreover, studies carried out on pups (AIZMAN *et al.* 1998) and human neonates GARCÍA DEL RÍO *et al.* 1982) preclude the direct involvement of aldosterone in the regulation of potassium excretion in the urine. It is likely that ANP antagonists modulate the kaliuretic action of the peptide in the studied calves. It is known from the literature that there is a functional interdependence between ANP and the renin-angiotensin-aldosterone system and vasopressin (AMADIEU-FARMAKIS *et al.* 1991; FAN *et al.* 1999; GEMELLI *et al.* 1991; OŻGO 2009).

The concentration of electrolytes in the blood of neonates depends on three variables: "initial" concentration determined during fetal life, intake from colostrum and milk, and excretion from the body (primarily by the kidney). Small changes in the blood plasma potassium concentration observed in the presented experiment primarily resulted from changes in glomerular filtration rate and tubular reabsorption, since the concentration of electrolyte in the blood after birth remained within the physiological range, and the feeding of the calves was standardized.

Literature data indicate that blood potassium concentration and its pattern of change in neonatal life may vary. BARANOW-BARANOWSKI *et al.* (1988) and ALBRYCHT *et al.* (1995) observed potassium concentrations of 5.63 mmol/l and 5.17 mmol/l, respectively, in calves during the first week of life, which was higher than that observed in the presented experiment. However, SKRZYPCZAK (1991) and OŻGO (2000) reported blood plasma potassium concentrations in calves similar to those obtained in our experiment: 4.25 mmol/l and 3.86 mmol/l, respectively, and a different pattern of change. The experiment showed slightly higher blood plasma concentrations of potassium in calves from the third day of life compared to those observed in the first two days of life. LORENZ *et al.* (1997) suggest that the increase in blood plasma potassium in neonates may be due to the transport of this ion from the intracellular to extracellular space.

The results of this study suggest that neonate calf kidneys are sufficiently prepared to regulate kalemia. Atrial natriuretic peptide is not directly involved in the regulation of tubular reabsorption of potassium in calves in the first week of life, although it is highly likely that the peptide is involved in the excretion of potassium in the urine in calves during the first seven days of life.

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