THE EFFECT OF SPIRONOLACTONE (ALDACTONE) ON ELECTROLYTE BALANCE AND RENAL FUNCTIONS OF CALVES

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Abstract

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A short spironolactone test was carried out in a group of 10 clinically healthy calves at the age of 4 weeks. For 5 days (every 24 hours) the calves were administered Aldactone (Searle), per os, at a dose of 1 mg/kg of body weight. Before the test began and 120 and 144 hours after giving the first spironolactone dose, the effective renal blood (ERBF) and plasma (ERPF) flow, and the glomerular filtration rate (GFR) were measured using sodium salt of p-aminohippuric acid and inulin. The levels of sodium, potassium and chlorides in plasma and erythrocytes were also determined. Some changes in the concentration of tested electrolytes were found in both the plasma and the intracellular fluid of erythrocytes. Changes in the renal function of calves were also indicated by an increase in effective renal plasma flow as well as by a decrease in glomerular filtration rate.

Spironolactone, electrolyte balance, renal function, calves

Calf kidneys are functionally efficient in the first month of life. However, they reveal some features of functional immaturity. These involve lowered effective renal blood (ERBF) and renal plasma (ERPF) flow, low glomerular filtration rate and low ability of urine concentration (Mercer et al. 1978; Wanner et al. 1981; Hartmann et al. 1987; Skrzypczak 1989; Skrzypczak et al. 1989; Skrzypczak 1991). The observed high tabular resorption of Na, K and Cl in the first 3–4 days of life (Safwate et al., 1980; Skrzypczak, 1991) becomes lower as the age of calves increases (Safwate et al. 1982; Skrzypczak 1989).

The results of experiments show that, by the third day of life, mechanisms which control sodium resorption become active and kidney tubules respond to aldosterone infusion with the growth of Na resorption (Safwate et al. 1980; Safwate et al. 1982; Itoh et al. 1985; Safwate 1985). Some authors, however, found a lack of correlation between the plasma renin activity and the aldosterone level, and sodium and potassium concentrations in the blood plasma (Siegler et al. 1977; Moncaup et al. 1980; Safwate et al. 1982). Cabello (1980) even reports a negative correlation between plasma levels of aldosterone and sodium. Jankowiak (1989) showed that administering DOCA at a dose of 0.1 mg/kg body weight i.m. caused a clearance drop and the urine excretion of sodium, potassium and chlorides also decreased. Safwate (1985) also noticed a lowering of sodium excretion in urine after aldosterone infusion, although he did not observe any changes in potassium excretion. Some authors indicate that there is a possibility of metabolic stimulation of the calf suprarenal glands in the first month of life (McEwan et al. 1968; Baranow-Baranowski et al. 1987).

As can be seen from the literature review, there are many issues connected with tubular activity regulation in the postnatal period pertaining to electrolytes resorption which have not been fully explained yet (Kagawa 1960; Braunlich and Kersten 1972; Corvol et al. 1981). The objective of this paper was to examine the effect of spironolactone (Aldactone) on electrolyte balance of body fluids and on glomerular filtration rate and effective blood and plasma flow through young calf kidneys.

Materials and Methods

The experiment was carried out on a group of 10 clinically healthy calves of cb. breed at the age of 4 weeks. They were kept in a calf-pen under constant, optimal conditions. Their left and right jugular vein had been catheterized and they had been weighed before the experiment began.

Prior to the treatment period, the effective renal plasma (ERPF) and blood (ERBF) flow and the glomerular filtration rate (GFR) were defined. The levels of sodium, potassium and chlorides in blood plasma and erythrocytes were examined. To assess ERPF and GFR, sodium salt of p-aminohippuric acid (Serva-GmbH) and inulin (Sigma Chem. Co.) were used respectively. The clearance of these substances was measured using Bettge's method. On the basis of ERPF and haematocrit, the amount of ERBF was defined and the filtration fraction (FF) was calculated. In order to block aldosterone activity, a short spironolactone test was conducted. The calves were administered 1 mg/kg body weight of Aldactone (Searle) per os for 5 days. After 120 and 144 hours from giving the first dose of Aldactone, new examinations of ERPF, GFR values and Na, K and Cl levels in plasma and whole blood were carried out.

The colorimetric method was used for determination of inulin levels based on the fructose amount (Tomaszewski, 1970), and Wangh and Beall's method was used to measure PAH plasma levels (Wangh and Beall 1974). Sodium and potassium concentrations were determined using the photometric method (Flapho-4) and chlorides were assessed using the potentiometric method (Chlorimetr Spexon-100). The concentration of ions in erythrocytes was calculated according to the following formula:

$$C_{er} = \frac{(C_{wb} - C_{pl})}{H_t + C_{pl}}$$

where: C_{er} = ion concentration in the erythrocytes, C_{pl} = concentration in plasma, C_{wb} = concentration in whole blood, H_t = haematocrit.

The values obtained were expressed per 1 m^2 of the body surface of calves according to the following formula:

$$S = 0.105\sqrt{m.c^2}.(m^2)$$

where: S = body surface, m. c. = body weight (Skrypczak 1989).

Statistical significances were calculated using D-Duncan's test.

Results and Discussion

The effect of administering Aldactone is that it blocks mineralocorticoid receptors in tubules and decreases aldosterone biosynthesis (Corvol et al. 1981) by lowering the number of open sodium canals (Horisberger and Giebisch 1987). The results obtained show that, in the calves, Aldactone caused a change in the mineral status, first of all in the extracellular fluid space.

The levels of Na, K and Cl in blood plasma and erythrocytes before the experiment were approximately the same as other authors have observed (Kucera et al. 1977; Safwate et al. 1982; Baranow-Baranowski et al. 1988). Aldactone administration caused a decrease of sodium level and an increase of K concentration in blood plasma ($P<0.01$). The concentration of chloride ions also decreased considerably although statistical differences at the $P < 0.05$ level were not obtained (Table 2).

Table 1

Glomerular filtration rate (GFR), effective renal plasma (ERPF) and blood (ERBF) flow, filtration fraction (FF) and haematocrit (Ht) in calves before and 120 and 144 hours after giving the first Aldactone dose (n=10, $\bar{x} \pm SD$)

PARAMETERS	HOURS OF EXPERIMENT		
	0	120	144
GFR	46.83	44.30	43.82
(ml/min/m²)	3.43	3.68	3.78
ERPF	297.49	286.67	286.51
(ml/min/m²)	28.36	26.27	33.28
ERBF	440.35	445.15	445.82
(ml/min/m²)	42.64	38.99	51.99
FF	15.79	15.48	15.37
(%)	0.70	0.76	1.00
Ht	0.32	0.36 **	0.36**
(1/1)	0.02	0.02	0.02

** Difference from pre-treatment value ($P \leq 0.01$)

Table 2

Sodium, potassium and chloride content in calves blood plasma before and 120 and 144 hours after giving the first Aldactone dose (n = 10, $\bar{x} \pm SD$)

ELECTROLYTES	HOURS OF EXPERIMENT		
	0	120	144
Na	132.00	128.10 **	127.40**
(mmol/l)	2.68	1.37	1.43
K	3.94	4.27 **	4.24**
(mmol/l)	0.12	0.16	0.17
Cl	103.18	100.28	99.96
(mmol/l)	3.46	2.37	2.26

** Difference from pre-treatment value ($P \leq 0.01$)

Some changes in the mineral profile of intracellular erythrocyte fluid were also recorded (Table 3). The inhibition of the antinatriuretic aldosterone effect lowered the concentration of sodium significantly.

Table 3

Sodium, potassium and chloride content in calf erythrocytes before and 120 and 144 hours after giving the first Aldactone dose (n = 10, x ± SD)

ELECTROLYTES	HOURS OF EXPERIMENT		
	0	120	144
Na	27.64	25.37 **	25.41 **
(mmol/l)	1.24	1.35	1.11
K	69.79	70.53	70.07
(mmol/l)	2.08	1.62	1.79
Cl	42.14	39.36	39.48
(mmol/l)	2.70	2.94	2.55

** Difference from pre-treatment value ($P \leq 0.01$)

The increase of the haematocrit indicator ($P < 0.01$) points to a decrease of blood plasma volume, which was probably caused by increased Na, Cl and water excretion in urine (Table 1).

The renal plasma and blood flow and the glomerular filtration rate before Aldactone administration (Table 1) had been at comparable levels with the results obtained by other authors (Meercer et al. 1976; Wanner et al. 1981; Hartman et al. 1967). In the experiment there was also an indication that the changes in mineral status and the changes in plasma volume, caused by Aldactone administration, modified the renal function. Although the significance of the changes in blood and plasma flow was not statistically confirmed at the $P < 0.05$ level, their biological importance in the whole process of maintaining water-electrolyte homeostasis was evident. It seems that the observed increase in blood flow through the kidneys (Table 1) is connected with the inhibition the renin-angiotensis system caused by an increase in the amount of sodium in distal tubules. Perhaps, this is due to changes in blood flow through the renal medulla. The lowered ERPF, in spite of increased ERBF, was connected with the decreased blood plasma volume. In parallel with the ERPF decrease, GFR also decreased, which is evident in the stable amount od the filtration fraction (Table 1). This renal response may constitute a „compensatory" mechanism which limits the amount of sodium chloride excreted in urine.

In conclusion, there appeared to be marked aldosterone activity in 4-week-old calves which could be inhibited by administration of Aldactone. This, in turn, caused increased renal excretion of Na and Cl leading to a decrease in their levels in blood plasma and erythrocytes. There was also a decrease in plasma volume. The water-electrolyte changes in the extracellular fluid affected renal function reversibly, modifying blood flow through the kidneys and the glomerular filtration rate. This constitutes a mechanism limiting electrolyte excretion in urine.

Účinek spironolaktonu (Aldaktonu) na rovnováhu elektrolytů a funkci ledvin u telat

U skupiny 10 klinicky zdravých telat ve stáří 4 týdnů byl proveden jednoduchý test inhibice aldosteronu spironolaktonem. Každých 24 hod. po dobu 5 dní jim byl perorálně podáván Aldacton, Searle, v dávce 1 mg/kg tělesné hmotnosti. Před počátkem experimentu a za 120 a 144 hodin po první dávce Aldactonu byl měřen průtok plasmy a krve ledvinami a rychlost glomerulární filtrace a stanoveny hladiny sodíku, draslíku a chloridů v plazmě a erytrocytech. Zjištěné změny v koncentracích elektrolytů v plazmě, v erytrocytech a u indikátorů renálních funkcí ukazují na výraznou roli aldosteronu ve funkci ledvin u telat ve věku 4 týdnů.

Воздействие спиронолактона (Альдактона) на равновесие электролитов и деятельность почек телят

На группе 10 клинически здоровых телят в возрасте 4 недель проводили простой тест торможения альдостерона спиронолактоном.

В течение 5 суток (каждые сутки) перорально вводили Альдактон, Сирле, дозой 1 мг/кг массы тела. Перед началом эксперимента и после 120 и 144 часов от первой дозы Альдактона проводили измерения протекания плазмы и крови почками и скорости гломерулярной фильтрации, а также определяли уровни натрия, калия и хлоридов в плазме и эритроцитах. Выявленные изменения в концентрации эритроцитов в плазме и эритроцитах, а также в индикаторах ренальных функций свидетельствуют о выразительной роли альдостерона в действии почек телят в возрасте 4 недель.

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