FOLIA POMERANAE UNIVERSITATIS TECHNOLOGIAE STETINENSIS
Folia Pomer. Univ. Technol. Stetin., Agric., Aliment., Pisc., Zootech. 2014, 312(31), 63–68

Alicja DRATWA-CHAŁUPNIK, Agnieszka HEROSIMCZYK

THE REGULATION OF CHLORIDE BALANCE IN CALVES DURING THE FIRST WEEK OF LIFE

REGULACJA BILANSU CHLORKÓW W OSOCZU KRWI CIELĄT W PIERWSZYM TYGODNIU ŻYCIA

Department of Physiology, Cytobiology and Proteomics, West Pomeranian University of Technology, Szczecin, Poland

Streszczenie. Badania przeprowadzono na 10 klinicznie zdrowych cieliczkach rasy polsko-fryzyjskiej odmiany czarno-białej, w ciągu pierwszych 7 dnia życia postnatalnego. Celem prezentowanych badań była analiza nerkowej regulacji bilansu chlorków podczas pierwszego tygodnia życia cieląt. Stężenie chlorków w osoczu krwi cieląt w pierwszym tygodniu życia wynosiło średnio 98,86 mmol $\cdot$ l^{-1} i mieściło się w granicach norm fizjologicznych. Do piątego dnia życia koncentracja tego elektrolitu była stabilna, a następnie w siódmym dniu życia nieznacznie się obniżyła. Przy ujednoliconym żywieniu (siarą i mlekiem matek) obserwowane zmiany w kolejnych dniach pierwszego tygodnia życia związane były głównie ze zmianami czynności nerek (przesączania w kłębkach i resorpcji kanalikowej). W pierwszym tygodniu życia cieląt obserwowano istotne zmiany wielkości ładunku przesączonego, resorpcji kanalikowej oraz wydalania chlorków z moczem. Analiza zmian wielkości ładunku przesączonego chlorków wskazuje, że zmiana stężenia chlorków w osoczu krwi nie miała wpływu na ten wskaźnik. Stwierdzono, że decydującym mechanizmem regulującym wydalanie chlorków z moczem są zmiany wielkości resorpcji tego elektrolitu w kanalikach nerkowych. Uzyskane wyniki wskazują, że nerki cieląt noworodków są dostatecznie przygotowane do regulacji stężenia chlorków w osoczu krwi.

Słowa kluczowe: filtracja kłębkowa, resorpcja i sekrecja (klirens) chlorków.
Key words: glomerular filtered, reabsorption and excretion (clearance) of chloride.

INTRODUCTION

Chloride is the major electrolyte of the extracellular fluid. Along with potassium and sodium plays important role in maintaining body fluid balance. Moreover, chloride regulates pH in the body, enabling normal muscle contraction and relaxation.

Corresponding author – Adres do korespondencji: PhD Alicja Dratwa-Chałupnik, Department of Physiology, Cytobiology and Proteomics, Faculty of Biotechnology and Animal Husbandry, West Pomeranian University of Technology, Szczecin, Doktora Judyma 6, 71-466 Szczecin, Poland, e-mail: Alicja.Dratwa-Chalupnik@zut.edu.pl

The kidneys maintain chloride homeostasis by regulating its reabsorption or excretion. It is estimated that approximately 50% of filtered chloride is reabsorbed by the proximal tubules. Channel activated by cyclic GMP is one of the chloride channels, which is regulated by ANP (atrial natriuretic peptide) and urodilatin (Darvish et al. 1995). NaCl reabsorption in the thick ascending limb of Henle's loop (TAL), is stimulated by cAMP, which is activated by antidiuretic hormones and is inhibited by cyclic GMP cascade, through activation of either guanylyl cyclase receptors (by ANP, urodilatin) or soluble guanylyl cyclase (by nitric oxide, NO) (Bailly 1998). ANP decreases chloride reabsorption in both luminal and basolateral tubular membranes along the TAL (Bailly 2000). Furthermore, sorting-protein-related receptor with A-type repeats (SORLA) expressed in the TAL epithelial cells, distal convoluted tubule, and the connecting tubule also regulates chloride transport. Lack of receptor expression in the TAL cells results in an inability to properly reabsorb sodium and chloride (Reiche et al. 2010). Sodium chloride reabsorption in the thick ascending limb mediated by Na-K-Cl cotransporter (NKCC2) is stimulated by the antidiuretic hormone vasopressin (Giménez and Forbush 2003). The Na-Cl cotransporter, located in the early distal convoluted tubule (DCT), is directly activated by the vasopressin (Gamba 2009; Mutig et al. 2010; Pedersen et al. 2010).

Above mentioned two antagonistic hormones (ANP and vasopressin) mainly participate in the chloride transport in the kidney. It is known that ANP regulates kidney electrolyte balance directly and indirectly i.a. by suppression of vasopressin secretion (Dratwa 2002). Our previous studies were aimed at explaining the participation of ANP in the regulation of sodium and potassium balance in newborn calves (Dratwa et al. 2004; Dratwa-Chałupnik et al. 2011). ANP increases glomerular filtration rate (GFR) and both salt and water excretion (Dratwa 2002), but these effects are not fully understood in newborn animals.

The aim of this study was to analyze renal regulation of chloride balance in calves during first seven days of life.

MATERIAL AND METHODS

The experiment was carried out on 10 clinically healthy, female Polish-Friesian var. Black-and-White calves, during the first seven days of postnatal life. During the study period, the animals were housed in individual pens under standardized environmental conditions. Calves were fed colostrum and mothers' milk (three times a day) in the amount of 6–7 liters per day.

Blood and urine samples were collected daily in accordance with previously described procedure (Dratwa 2006). The potentiometric method was used to determine the plasma and urine chloride concentration (chlorimeter Spexon).

In order to assess kidney's ability to regulate chloremia, the glomerular filtered load of chloride (F_{Cl}), the load of excreted with urine, as well as chloride reabsorption were calculated, according to the following formulas:

$$F_{Cl} = P_{Cl} \cdot GFR \; [\text{mmol} \cdot \text{l}^{-1}]$$

$$TR_{Cl} = \frac{F_{Cl} - (U_{Cl} \cdot V)}{F_{Cl}} \cdot 100 \; [\%]$$

$$C_{Cl} = \frac{U_{Cl} \cdot V}{P_{Cl}} \; [\text{ml} \cdot \text{min}^{-1}]$$

where:

F_{Cl} – glomerular filtered load of chloride,
P_{Cl} – blood plasma chloride concentration [mmol · l^{-1}],
GFR – glomerular filtration rate [ml · min^{-1}],
TR_{Cl} – chloride tubular reabsorption,
U_{Cl} – urine chloride concentration [mmol · l^{-1}],
C_{Cl} – chloride clearance,
V – minute diuresis [ml · min^{-1}].

The resulting data were standardized for 1 m^2 of the body surface area. Mean values and standard deviations were calculated. The resulting data were analysed using an ANOVA with repeated measurements and Duncan's multiple range post hoc test (software: Statistica 10^{TM}) in order to test the significance of differences.

RESULTS

The mean blood plasma chloride concentration during the first week of calves' life was 98.86 mmol · l^{-1} (Table1).

Table 1. Mean concentration of chloride filtered load (F_{Cl}), chloride tubular reabsorption (TR_{Cl}), chloride excretion in the urine ($U \cdot V_{Cl}$), chloride clearance (C_{Cl}) blood plasma chloride concentration (P_{Cl}) in calves in the first week of life and standard deviation (SD) and significant differences between values in the following days of life
Tabela 1. Średnia koncentracja ładunku przesączonego chlorków (F_{Cl}), wielkość resorpcji kanalikowej chlorków (TR_{Cl}), wielkość wydalania chlorków ($U \cdot V_{Cl}$), wielkość klirensu chlorków (C_{Cl}), koncentracja chlorków w osoczu krwi (P_{Cl}) cieląt w pierwszym tygodniu życia oraz odchylenie standardowe (SD) i istotność różnic pomiędzy średnimi wartościami w kolejnych dniach życia

Specification Parametr		Day of life Dzień życia							Significance of differences Istotność różnic	
		1	2	3	4	5	6	7	p ≤ 0.01	p ≤ 0.05
F_{Cl}	$\overline{x}$ [mmol · min^{-1} · m^{-2}]	3.54	5.04	5.33	4.99	5.23	4.81	4.87	*1 → 2−7*	*3 → 4*
	SD	0.64	0.61	0.50	0.77	0.81	0.67	0.62		
TR_{Cl}	$\overline{x}$ [%]	98.73	98.59	97.54	97.01	95.75	96.41	97.96	*1 → 5, 6* *2 → 4, 5* *6 → 7*	*2 → 6* *3 → 5* *5 → 7*
	SD	1.23	1.56	2.20	2.32	1.84	1.60	1.42		
$U \cdot V_{Cl}$	$\overline{x}$ [μmol · min^{-1} · m^{-2}]	39.19	59.87	103.13	115.70	172.94	129.60	74.71	*1 → 5, 6* *2 → 5* *5 → 7* *6 → 7*	*1 → 4* *2 → 4, 6* *3 → 5*
	SD	40.87	64.08	91.17	89.22	72.98	46.77	39.62		
C_{Cl}	$\overline{x}$ [ml · min^{-1} · m^{-2}]	0.39	0.58	1.00	1.14	1.74	1.36	0.81	*1 → 5, 6* *2 → 5* *5 → 7*	*1 → 4* *2 → 4, 6* *3 → 5* *6 → 7*
	SD	0.41	0.60	0.85	0.86	0.71	0.53	0.47		
P_{Cl}	$\overline{x}$ [mmol · l^{-1}]	99.25	100.96	10162	101.22	98.63	96.07	94.29	*1 → 7* *2 → 6,7* *3 → 6, 7* *4 → 7* *6 → 7*	*1 → 6* *4 → 6* *5 → 7*
	SD	3.15	4.50	344	4.29	5.79	4.38	4.56		

The concentration of this electrolyte was stable until the fifth day of life ($\overline{x}$ = 100.34 mmol · l^{-1}), and was followed by a decrease to the value of 94.29 mmol · l^{-1} on the seventh day of life. The observed changes were statistically significant.

The lowest mean value of chloride filtered load was observed on the first day of calves' life, F_{Cl} = 3.54 mmol · min^{-1} · m^{-2} (Table 1). A significant (p ≤ 0.01) increase in this parameter was observed on the second day of life, and was followed by its stabilization in the following days of the first week of life ($\overline{x}$ = 5.04 mmol · min^{-1} · m^{-2}).

Tubular chloride reabsorption during the first week of calves' life demonstrated statistically significant changes (p ≤ 0.05). This parameter was stable and showed higher concentration (mean 98.66%) during the first two days of life (Table 1). In the following days, the parameter significantly (p ≤ 0.01) decreased, reaching the lowest value on the fifth (95.75%) and sixth (96.41%) day of life. On the seventh day of calves' life chloride tubular reabsorption increased significantly (p ≤ 0.01) to 97.96 %.

The direction of changes in the urinary chloride excretion was in accordance with changes in chloride clearance (Table 1). Clearance values significantly (p ≤ 0.01) increased until the fifth day of life and subsequently gradualy decreased until the end of experimental period. Furthermore, a great individual variability in renal excretion of chloride was indicated.

DISCUSSION

Blood plasma chloride levels in the newborn calves observed in the present study are within the reference values. These results are consistent with the previous report of Ożgo (2000), who determined the mean plasma chloride concentration on the level of 98.59 mmol · l^{-1}. However, plasma chloride levels demonstrated in the present experiment are higher than reported by Herosimczyk et al. (2011) – mean value of 91.09 mmol · l^{-1}. Moreover, both above mentioned authors observed a gradual decrease in blood plasma chloride concentration during the first week of calves' life (Ożgo 2000; Herosimczyk et al. 2011). Statistically significant increase in blood plasma ANP on the second and sixth day, determined in previous studies (Dratwa 2006), didn't influence blood plasma chloride concentration.

Due to the fact that the feeding was standardized (dam's colostrum and milk), the changes in concentration of plasma chloride in the following days of the first week of calves life were mainly associated with renal activity (glomerular filtration and tubular reabsorption).

Significant changes in glomerular filtration load, tubular reabsorption and urine excretion of chloride were recorded during the first week of life.

The values of the filtered load of chloride were not influenced by changes in blood plasma chloride concentration.

The results of the present study indicate that changes in chloride tubular reabsorption represent crucial mechanism responsible for urinary chloride excretion. Nevertheless, Ożgo (2009) observed lowering of both chloride tubular reabsorption values and urinary excretion of this electrolyte in the sixth and seventh day of calves' life. According to the authoress, the magnitude of changes in glomerular filtration load of chloride have a significant influence on the chloride elimination through the kidneys at the end of the first week of calves' life.

The observed decrease in tubular reabsorption and an increase in urine excretion until the fifth day of life didn't influence the chloride blood plasma concentration. Probably decrease in this electrolyte in blood, observed from fifth to sixth day of calves' life, caused the increase in tubular reabsorption and decrease in urine excretion of chloride. Kidney response on decrease in blood chloride is crucial to keep chloride balance.

Atrial natriuretic peptide regulates transport of the chloride ions along the renal tubules in the direct manner (Darvish et al. 1995; Bailly 1998). However, indirect role of this peptide in the regulation of the chlorides cannot be excluded as ANP inhibits the release of the RAA (renin-angiotensin-aldosterone system) hormones and also regulates kidney function in response to vasopressin. Above mentioned antinatriuretic and antidiuretic hormones participate in the NaCl transport (Nonoguchi et al. 1992; Bailly 1998; Dratwa 2002, 2004; Gamba 2009; Mutig et al. 2010; Pedersen et al. 2010). Atrial natriuretic peptide is a cardiac hormone, which stimulates natriuresis and diuresis via both receptor-A (ANRA) and guanylyl cyclase (GC)- linked receptor (Misono et al. 2011). The previous studies clearly indicate that ANP requires the presence of chloride to bind to the ANRA (Misono 2000; Ogawa et. al 2010).

RECAPITULATION

In conclusion of the conducted experiment, it can be said that the changes in concentration of plasma chloride in the following days of the first week of life were mainly associated with the glomerular filtration and tubular reabsorption. The values of the filtered load of chloride were not influenced by changes in plasma chloride concentration. The results of the present study indicate that changes in chloride tubular reabsorption represent crucial mechanism responsible for urinary chloride excretion.

Present results indicate that neonate calf' kidneys are sufficiently prepared to regulate chloremia.

REFERENCES

Bailly C. 2000. Effect of luminal atrial natriuretic peptide on chloride reabsorption in mouse cortical thick ascending limb: inhibition by endothelin. J. Am. Soc. Nephrol. 11, 1791–1797.

Bailly C. 1998. Transducting pathways involved in the control of NaCl reabsorpion in the trick ascending limb of Henle's loop Kidney. Int. Suppl. 65, 29–35.

Darvish N., Winaver J., Dagan D. 1995. A novel cGMP-activated Cl- channel in renal proximal tubules. Am. J. Physiol. 268, F323–329.

Dratwa A. 2002. Przedsionkowy peptyd natriuretyczny – ANP [Atrial natriuretic peptide – ANP]. Med. Weter. 58, 108–111. [in Polish]

Dratwa A. 2006. Atrial natriuretic peptide and renal haemodynamics in newborn calves. Acta Vet. Brno 75, 477–483.

Dratwa A., Ożgo M., Skrzypczak W.F. 2004. Udział przesionkowego peptydu natriuretycznego w regulacji natriurezy i diurezy cieląt noworodków (in: Noworodek a środowisko). Wrocław, ELMA, 7–20. [in Polish]

Dratwa-Chałupnik A., Ożgo M., Herosimczyk A., Lepczyński A., Michałek K., Skrzypczak W.F. 2011. Renal regulation of potassium homeostasis in calves in the first week of life including the role of Atrial Natriuretic Peptide. Folia Biol. Krak. 59, 157–161.

Gamba G. 2009. The thiazide-sensitive Na+-Cl⁻ cotransporter: molecular biology, functional properties, and regulation by WNKs. Am. J. Physiol. Renal Physiol. 297, F838–848.

Giménez I., Forbush B. 2003. Short-term stimulation of the renal Na-K-Cl cotransporter (NKCC2) by vasopressin involves phosphorylation and membrane translocation of the protein. J. Biol. Chem. 278, 26 946–26 951.

Herosimczyk A., Lepczyński A., Dratwa-Chałupnik A., Kurpińska A., Klonowska A., Skrzypczak W.F. 2011. Age-related changes of selected blood biochemical indicators in dairy calves during their first week of life. Folia Biol. Krak. 59, 25–30.

Misono K.S. 2000. Atrial natriuretic factor binding to its receptor is dependent on chloride concentration: A possible feedback-control mechanism in renal salt regulation. Circ. Res. 86, 1135–1139.

Misono K.S., Philo J.S., Arakawa T., Ogata C.M., Qiu Y., Ogawa H., Young H.S. 2011. Structure, signaling mechanism and regulation of the natriuretic peptide receptor guanylate cyclase. FEBS J. 278, 1818–1829.

Mutig K., Saritas T., Uchida S., Kahl T., Borowski T., Paliege A., Böhlick A., Bleich M., Shan Q., Bachmann S. 2010. Short-term stimulation of the thiazide-sensitive Na+-Cl⁻ cotransporter by vasopressin involves phosphorylation and membrane translocation. Am. J. Physiol. Renal Physiol. 298, F502–509.

Nonoguchi H., Tomita K., Marumo F. 1992. Effects of atrial natriuretic peptide and vasopressin on chloride transport in long- and short-looped medullary thick ascending limbs. Clin. Invest. 90, 349–357.

Ogawa H., Qiu Y., Philo J.S., Arakawa T., Ogata C.M., Misono K.S. 2010. Reversibly bound chloride in the atrial natriuretic peptide receptor hormone-binding domain: possible allosteric regulation and a conserved structural motif for the chloride-binding site. Protein Sci. 19, 544–557.

Ożgo M. 2000. Zależność między stężeniem AVP I elektrolitami we krwi cieląt w okresie neonatalnym [Relationship between AVP concentration and electrolytes in calves blood during the neonatal period]. Folia Univ. Agric. Stetin. 39, 119–124. [in Polish]

Ożgo M. 2009. Udział enzymu konwertującego w regulacji czynności nerek noworodków cieląt. Szczecin, ZUT. [in Polish]

Pedersen N.B., Hofmeister M.V., Rosenbaek L.L., Nielsen J., Fenton R.A. 2010. Vasopressin induces phosphorylation of the thiazide-sensitive sodium chloride cotransporter in the distal convoluted tubule. Kidney Int. 78, 160–169.

Reiche J., Theilig F., Rafiqi F.H., Carlo A.S., Militz D., Mutig K., Todiras M., Christensen E.I., Ellison D.H., Bader M., Nykjaer A., Bachmann S., Alessi D., Willnow T.E. 2010. SORLA/SORL1 functionally interacts with SPAK to control renal activation of Na(+)-K(+)-Cl(-) cotransporter 2. Mol. Cell. Biol. 30, 3027–3037.

Abstract. The experiment was carried out on 10 clinically healthy, female Polish-Friesian var. Black-and-White calves, during the first seven days of postnatal life. The aim of this study was to analyze renal regulation of chloride balance in calves during the first seven days of life. The mean blood plasma chloride concentration during the first week of calves' life was 98.86 mmol $\cdot$ l^{-1} and was within the physiological reference values. The concentration of this electrolyte was stable until the fifth day of life, and was followed by a slight decrease on the seventh day of life. Due to the fact that the feeding was standardized (dam's colostrum and milk), the changes in concentration of plasma chloride in the following days of the first week of life were mainly associated with the renal activity (glomerular filtration and tubular reabsorption). Significant changes in glomerular filtration load, tubular reabsorption and urine excretion of chloride were recorded during the first week of life. The values of the filtered load of chloride were not influenced by changes in plasma chloride concentration. Our results indicate that changes in chloride tubular reabsorption represent crucial mechanism responsible for urinary chloride excretion. The obtained results show that neonate calf' kidneys are sufficiently prepared to regulate blood chloride level.