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ATRIAL NATRIURETIC PEPTIDE AND VOLEMIA REGULATION IN NEWBORN CALVES

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ABSTRACT

The experiment was carried out on 10 clinically healthy Black-and-White calves during the first seven days of postnatal life. The concentration of ANP in blood plasma was determined with radioimmunoassay. The molality of blood plasma and urine was measured and osmolar clearance, free-water clearance, and free-water reabsorption were calculated.

The concentration of atrial natriuretic peptide in blood plasma of calves is low after birth and increases significantly during the first week of life. The decrease of blood plasma osmotic pressure, increase of osmolar clearance, free-water reabsorption, and urine flow during the first three days may indicate diuretic properties of ANP.

Key words: atrial natriuretic peptide, osmolar clearance, free-water reabsorption, urinary flow, newborn calves.

INTRODUCTION

In mammals, the atrial natriuretic peptide is synthesised by, stored in, and released mainly by the cardiac atrial myocytes. Increased tension of the atrial walls in response to elevated hydrostatic blood pressure is what triggers the ANP release [31]. Findings reported by many authors have demonstrated ANP release to the blood may also result from increased volume of the circulating blood. This can be concluded from the studies by Chapman et al. [8], carried out on pregnant women, as well as by Grant et al. [16], carried out in humans with experimentally elevated volume of blood plasma. Also Chevalier et al. [9], who studied rats, both young ones (25-30 days) and older ones (45-50 days of age), with experimentally elevated volume of blood plasma, also found an increased level of this hormone in blood. This has also been confirmed by Bierd et al. [5] on human infants; lower ANP concentrations in blood plasma were found with reduced volume of circulating blood.

Water may constitute about 80% of the body weight of a newborn calf. Skrzypczak [29] has demonstrated that the total blood volume remains relatively stable within the first 3-4 days of life, and the decrease in the total water observed from the fourth day results mainly from a decrease the extracellular fluid volume. Vasopressin is the hormone that retains water in the organism; however, despite its increase in the blood plasma observed during the first week of life, which was observed by Ożgo [22], the hormone did not efficiently prevent the organism from water loss. The effect of this antidiuretic hormone may be outweighed by a hormone of the opposite nature, possibly the natriuretic peptide. It has been demonstrated that the peptide, if intravenously administered to animals, enhances the excretion water with urine [1, 7, 14, 21, 25, 28].

This study may lead to explanation of the ANP participation in the regulation of constant water volume in newborn calves.

MATERIAL AND METHODS

The experiment was carried out on 10 clinically healthy Black-and-White calves (the fraction of Holstein-Friesian genotype higher than 80%) during the first seven days of their postnatal life. After the necessary zootechnical procedures and feeding with colostrum, the calves were transported to the research facility of the Department of Animal Physiology. During the experiment, the animals remained in individual boxes in uniform environments. The calves were fed on colostrum and 6-7 litters of maternal milk per day (three times a day).

Before the experiment, Foley catheters were inserted into the urinary bladders of the calves in order to collect urine in specified time intervals, while their external jugular veins were catheterised for blood sampling without causing unnecessary stress to the animals. The calves were weighed each day before the samplings, which took place at the same time of the day, one hour after morning feeding (at 9.00).

Urine was collected in two periods of time in order to measure per-minute urine flow (diuresis). Blood was collected to EDTA tubes (Vacuette with 1.8 mg EDTA-K_3 per 1 ml blood; Greiner Bio-One, Austria), in order to measure ANP concentration, and to heparin tubes (Heparin, Biochemie, Austria), in order to determine blood plasma molality. Blood samples were immediately centrifuged at 3000 rpm at 4°C for 15 min.

The molality of blood plasma and urine was measured on the collection with the cryoscopic method by means of a Knauer osmometer. On the other hand, the blood plasma which was to be used later for ANP assay was stored at –20°C until the analyses. The concentration of atrial natriuretic peptide was measured by means of radioimmunoassay, based on the concentrations of ^{125}I-labelled ANP, using a Shionoria ANP kit, CIS Bio Intl, France [12]. The radioactivity of the samples was measured for 60 sec. in a Wizard 1470 gamma spectrometer. ANP concentrations in the analysed samples were read from the standard curve.

The results allowed us to calculate osmolar clearance (C_{osm}), free-water clearance (C_{H_2O} = V-C_{osm}), and free-water reabsorption ($T^C_{H_2O}$ = C_{osm}-V).

The data obtained were standardised per 1 m^2 of calf body surface area, according to Meeh's formula [after Ketz, 18]:

$$S = 0.105 \cdot \sqrt[3]{mc^2} \ [m^2]$$

where:

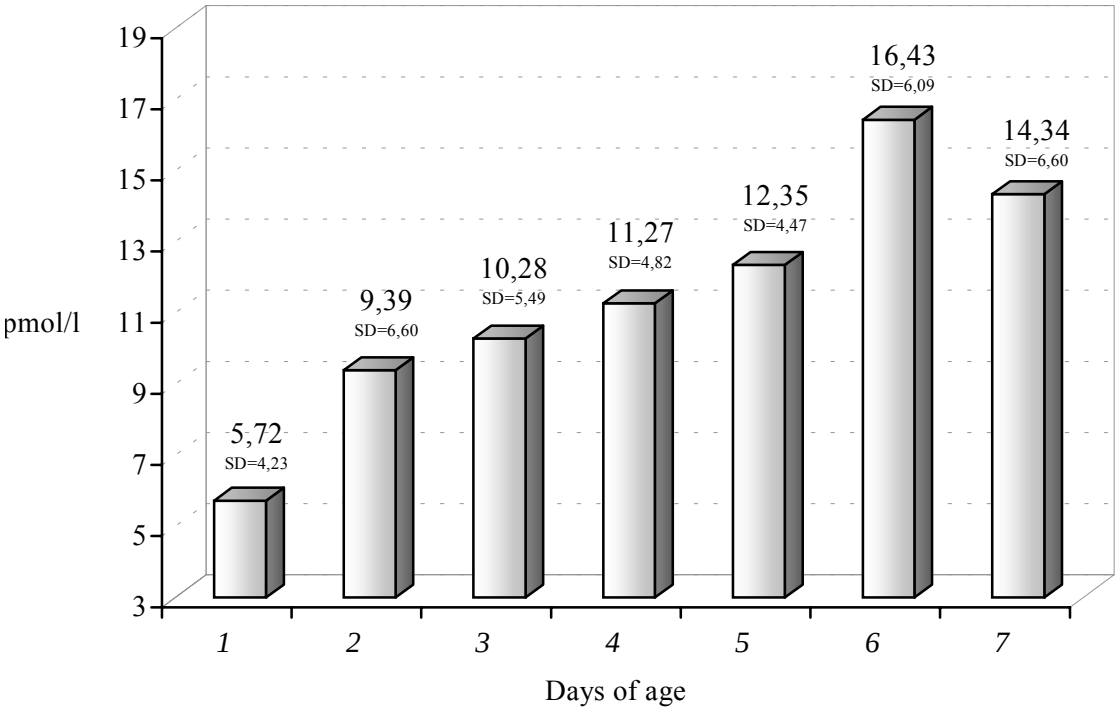
S – body surface area;
bw – body weight.

The results obtained were used to calulate means and standard deviations. In order to estimate the significance of differences, we used ANOVA with replications. Relationships between the concentration of atrial natriuretic peptide in blood plasma and the tested indices of renal function in the subsequent days of the calves' postnatal life were estimated with the coefficient of correlation. Statistical computations were performed by means of Statistica 6.0 software package.

RESULTS

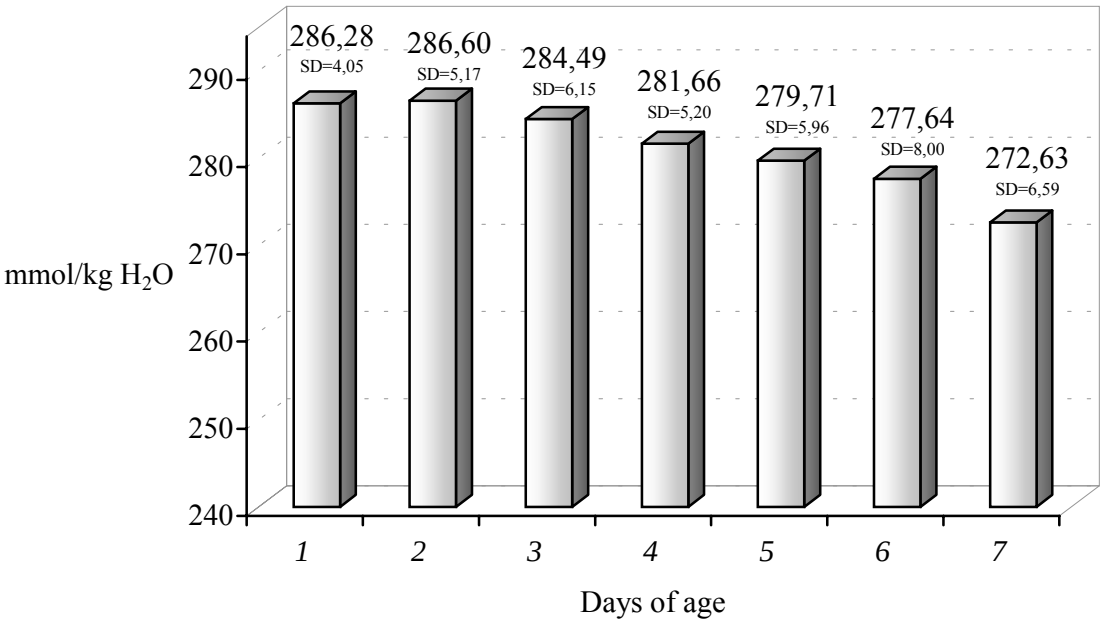
The calf blood plasma ANP concentration increased significantly ($p \leq 0.01$) during the first seven days of life (Figure 1). On the first day postpartum, the concentration of this hormone was 5.72 pmol/l, reaching 14.34 pmol/l on the 7th day. The highest blood plasma concentration of ANP was recorded on the sixth day (16.43 pmol/l). A significant observation is that the concentration of this hormone in blood plasma increased on the 2nd day and the 6th day of life of the calves. The mean ANP concentration in blood plasma for the first week of life was 11.40 pmol/l; however, heavy individual differences were found in the concentration of the hormone.

Figure 1. Concentration of ANP in the blood plasma of the calves



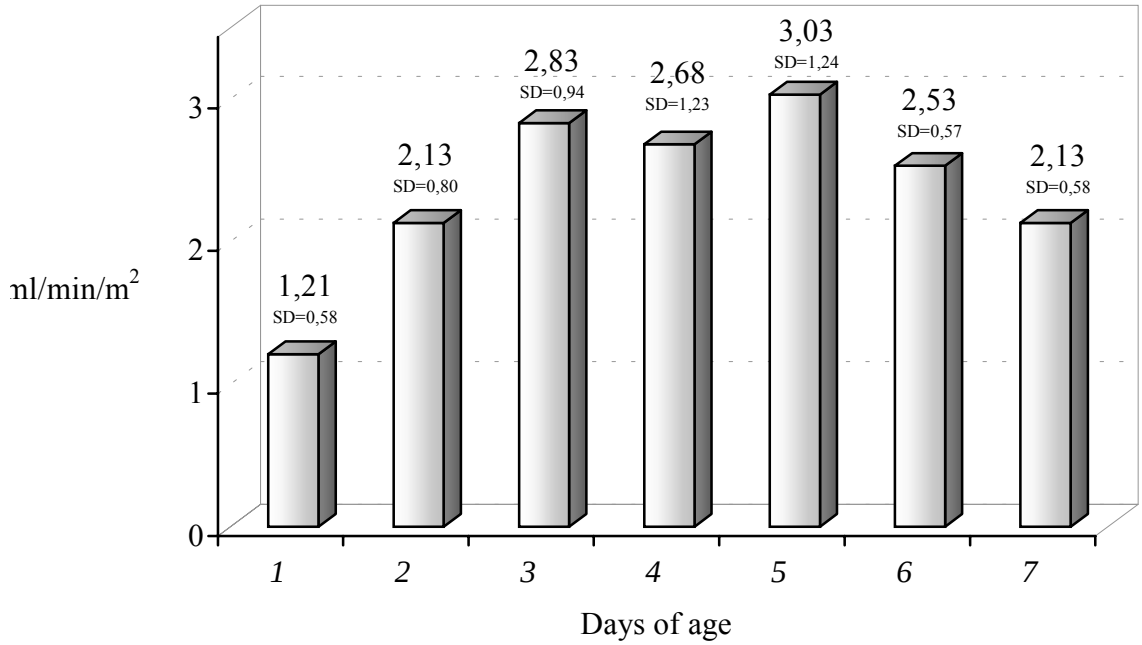
The mean molality of the blood plasma during the first week of life was 281.29 mmol/kg H_2O (Figure 2). The experiment has demonstrated that blood osmotic pressure decreased from 286.28 mmol/kg H_2O (the first day of life) to 272.63 mmol/kg H_2O (the seventh day of life). The changes were found statistically significant ($p \leq 0.01$). It should be noted that blood plasma molality remained relatively stable over the first three days of life – there were no statistically significant differences at $p \leq 0.05$.

Figure 2. Osmotic pressure (P_{osm}) of the blood plasma of the calves



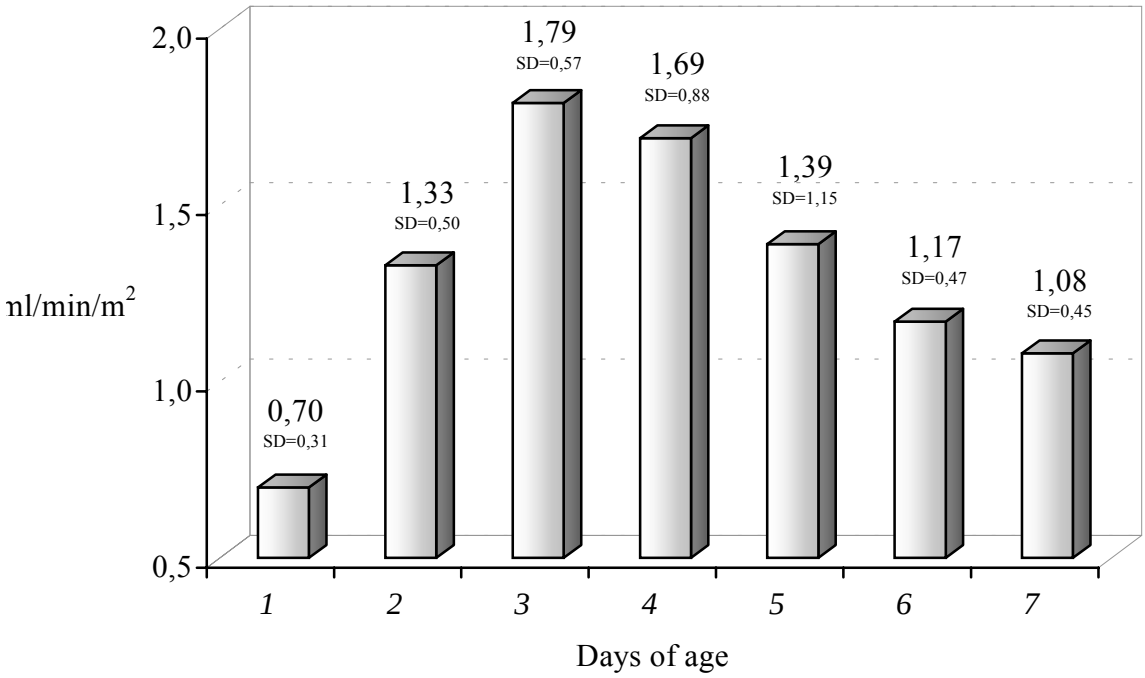
The osmolar clearance represents the index of osmoles excretion. In the present experiment, the parameter ranged between 1.21 ml/min/m^2 (the first day of life) and 3.03 ml/min/m^2 (the fifth day). The differences between these values were statistically significant ($p \leq 0.01$). It should also be noted that osmolar clearance increased significantly ($p \leq 0.01$) over the first three days of life and stabilised relatively in the remaining days (Figure 3).

Figure 3. Osmolar clearance (C_{osm}) in calves



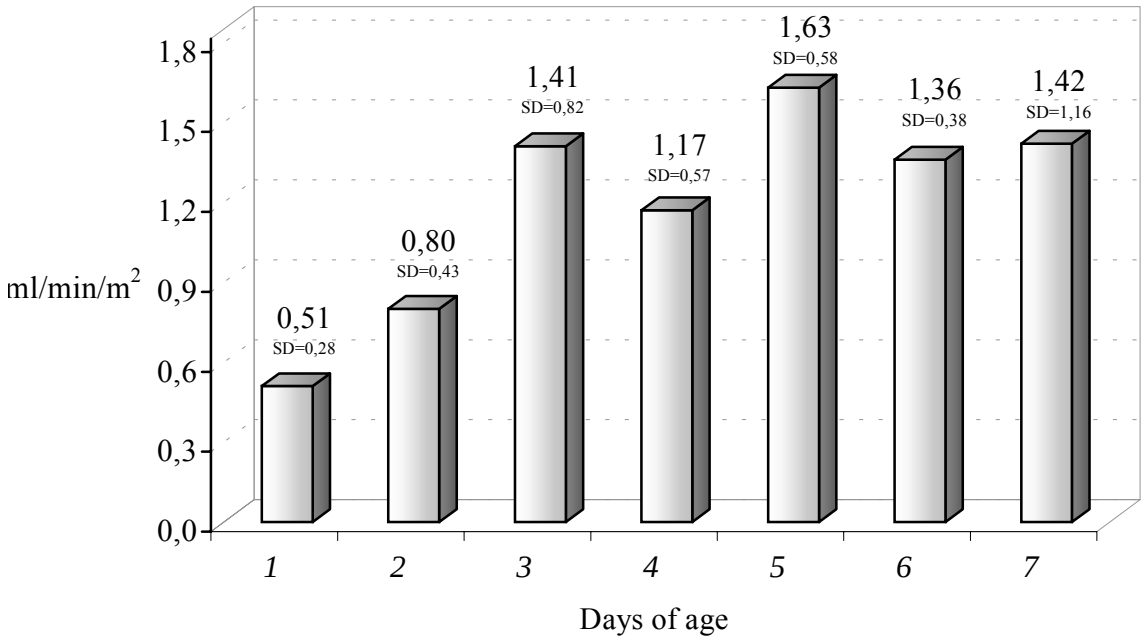
The free-water reabsorption is a parameter informing about the "net" water reabsorption in renal tubules. The parameter increased significantly ($p < 0.01$) from 0.70 ml/min/m^2 (the first day) to 1.79 ml/min/m^2 (the third day). Over the following days of the first week of life, the index significantly decreased ($p \leq 0.05$, Figure 4).

Figure 4. Free-water reabsorption ($T^C_{H_2O}$) in calves



The undesirable osmotically active substances are excreted from the blood plasma with various volumes of urine. In the present experiment, the diuresis was the lowest on the first day of life (0.51 ml/min/m^2) and increased significantly ($p \leq 0.01$) until the third day (1.41 ml/min/m^2), to finally stabilise at an average level of 1.39 ml/min/m^2 (Figure 5).

Figure 5. Urine flow (V) in calves



No correlation was found between the changes in ANP concentrations in the blood plasma and the changes in blood plasma osmotic pressure, osmolar clearance, reabsorption water, or urine flow.

DISCUSSION

The available literature describes various patterns of changes of ANP concentration in the neonatal blood plasma. The age-related increase in the newborn calves blood plasma ANP concentration observed in our experiment has been confirmed by Tulassay et al. [33] and Gemelli et al. [15], who studied the effect on human neonates. A reversed pattern in ANP concentration changes in the blood plasma of calves was reported by Takemura et al. [32]. Also Amadieu-Farmakis et al. [2, 3] observed the highest concentration of ANP in calf blood plasma directly post-partum, which was followed by a decrease until the third day of age. On the remaining days of the first week, the authors recorded a slightly growing trend.

It seems that a number of factors may have influenced the increase in ANP in the blood plasma of calves with age which we observed in our experiment. It is known that the main factors enhancing the release of ANP include elevated volume and/or pressure of circulating blood [8, 9, 31]. This has been also confirmed by Grant et al. [16], who observed that experimentally elevated plasma volume in adult men led to increased concentration of ANP in blood. Chevalier et al. [10] have demonstrated that the renal response to ANP in rats with experimentally elevated plasma volume increases with age during the postnatal period. It has also been found that total water volume in calves younger than one week is high, 80% of body weight on average [29], and that high concentration of ANP in blood plasma of human neonates during the first 24 hours of life is correlated with a high diastolic and systolic pressure [15].

Probably, the high molality of calf blood plasma during the first three days was one of the factors that influenced the synthesis and release of ANP from cardiac atrial myocytes. This may be confirmed also by Kamoi et al. [19], who demonstrated that secretion of ANP in adult humans was regulated mainly by changes in blood plasma volume, modulated by changes in osmotic pressure. Both factors, according to the authors, are also responsible for vasopressin release (an antidiuretic, antagonistic to ANP). Results reported by Clark et al. [11], who studied adult humans, indicate that ANP may inhibit the antidiuretic activity of vasopressin in response to a hypertonic solution infusion.

The present experiment has shown that calf blood plasma molality decreased during the first week of life. The reduction in molality of calf blood plasma with age was also observed by Ożgo [24] and Skrzypczak [30]. On the other hand, Safwate et al. [26], in lambs, and Muszczyński et al. [20], in goats, did not find significant differences in blood plasma molality during the first week of life.

An analysis of changes in the plasma osmotic pressure, osmolar clearance, and free-water reabsorption has proved that calf kidneys have strong ability to regulate isotonicity. The blood plasma osmotic pressure, which decreases from the 3rd or 4th day of age, results in reduction of osmolar clearance and free-water reabsorption.

Results by many authors indicate that urine flow in neonates is low and increases along with the individual development [4, 6, 26]. In the present studies, a significant ($p \leq 0.01$) increase in urine flow within the first three days was found. These changes were convergent with the changes in atrial natriuretic peptide, which may indicate the diuretic activity of the hormone. The results of studies by Cuneo et al. [13] and Janssen et al. [17] on humans, Amadieu et al. [1] on calves, Nushiro et al. [21] and Seino et al. [27] on rabbits, and Rakotondrazafa et al. [25] on adult rats, confirm the diuretic properties of ANP. It should be noted that osmolar clearance increased significantly ($p \leq 0.01$) within the first three days of life of calves. Parallel increase in free-water reabsorption indicates the urine concentration. However, increasing urine flow reflects the enhanced water removal from the organism with urine. This would confirm the results by Skrzypczak [29], who observed highly significant reduction in the amount of extracellular fluid volume in calves during the first week of life despite, which has been demonstrated by Ożgo [23], the increasing vasopressin concentration during this period of life. Tulassay et al. [33] suggest that ANP is important in volemia regulation during the postnatal life. The authors suggest that atrial natriuretic peptide is responsible for decrease extracellular fluid volume.

It should be noted that no convergence was observed between changes in urine flow and the changes in blood plasma ANP concentration between the 4th and the 7th day of age (non-significant coefficients of correlation at $p \leq 0.05$). During this period, a relatively stable urine flow was recorded despite a decrease in osmolar clearance (the significance of changes were not confirmed at $p \leq 0.05$) and a significant decrease in free-water reabsorption.

CONCLUSIONS

The concentration of atrial natriuretic peptide in blood plasma of calves is low after birth and increases significantly during the first week of life. The changes in blood plasma osmotic pressure, osmolar clearance, free-water reabsorption, and urine flow during the first three days may indicate diuretic properties of ANP. No relationship between the studied renal indices and the concentration of atrial natriuretic peptide from the fourth until the seventh day of calf life may indicate that the diuretic properties of ANP are “equalised” by antidiuretic agents. It seems that the role of diuretic and antidiuretic hormones in the regulation of volemia in calves is determined by the water-electrolyte balance on the moment of birth.

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