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Research Article

The Levels of Trace Elements and Macrominerals in Calves with Sepsis [1]

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Abstract

The aim of this study was to determine the levels of macrominerals and trace elements in the blood of newborn calves with sepsis. The study was carried out on a total of 30 calves, aged 2-35 days old, of which 25 with sepsis and 5 healthy. In clinical examination, prolonged capillary refill time and tachypnea were observed in calves with sepsis. The levels of Cu, K, P and S in calves with sepsis were higher compared to the control group, and the levels of Na, total and ionized Ca, Fe and Zn were also lower compared to the control group. In conclusion, in this study, significant increase in K and Cu concentrations and significant decrease in Na and Ca concentrations were found in calves with sepsis. According to the results, K, Cu, Na and Ca may have important roles in the pathophysiology of sepsis.

Keywords: *Calves, Macromineral, Sepsis, Trace elements*

Sepsisli Buzağılarda İz Elementler ve Makrominerallerin Seviyeleri

Öz

Bu çalışmanın amacı, sepsisli yenidoğan buzağılarda makromineraller ve iz elementlerin seviyelerini belirlemektir. Çalışma, 2-35 günlük, 25'i sepsisli ve 5'i sağlıklı olan toplam 30 buzağı üzerinde gerçekleştirildi. Klinik muayenede sepsisli buzağılarda kapiller geri dolum süresinde uzama ve takipne gözlendi. Kontrol grubu ile karşılaştırıldığında sepsisli buzağıların Cu, K, P ve S düzeyleri yüksek, Na, total ve iyonize Ca, Fe ve Zn düzeyleri düşüktü. Sonuç olarak, bu çalışmada sepsisli buzağılarda K ve Cu konsantrasyonlarında önemli artış, Na ve Ca konsantrasyonlarında ise anlamlı azalma olduğu tespit edilmiştir. Bu sonuçlar doğrultusunda K, Cu, Na ve Ca'un sepsisin patofizyolojisinde önemli bir rolü olabileceği değerlendirildi.

Anahtar sözcükler: *Buzağı, Makromineral, Sepsis, İz elementler*

INTRODUCTION

Septicemia is the presence of a pathogenic bacterium in circulation and different organs and systems. Septicemia in newborn farm animals is usually associated with *E. coli* and *Salmonella* spp., which are significant morbitiy and mortality causes [1]. *E. coli* is a bacterium that is the most commonly isolated from blood circulation in septicemic calves [2-4], however, gram positive bacteria have been determined in 10% of septicemic calves, and polymicrobial infection in 28% [5]. Failure of passive transfer of colostral immunoglobulins is a high risk for bacterial infection [1,6,7].

For proper growth of animals and continuation of reproductive functions, inorganic elements are essential. Calcium, phosphorus, sodium, chlorine, potassium, magnesium and sulfur are found in large amounts in an organism. These elements have significant functions in body. The elements that are less needed by the organism are called trace minerals. These elements are: cobalt, copper, iodine, ferrous, manganese, molybdenum, selenium, zinc, fluorine, chromium, etc. The trace minerals are the components of some important hormones or enzyme cofactors with metalloenzyme [8,9]. The inflammatory conditions cause significant changes in the levels of trace elements and macro minerals.

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These changes are the result of the reaction of the organism to an inflammatory response [10-12]. Ranjan et al.[11] found a significant increase in blood copper level and a significant decrease in zinc level in calves with diarrhea compared to healthy calves. In addition, endotoxemia in cattle has been reported to cause a decrease in zinc and calcium levels [10]. Furthermore, hyponatremia and hyperkalemia are common findings in dehydrated and endotoxemic neonatal ruminants [13].

Significant changes in micro and macro elements were observed in patients with systemic inflammatory response syndrome (SIRS), sepsis and many critical diseases in human medicine. We assumed that sepsis in calves may cause changes in trace elements and macrominerals. Therefore, the aim of this study was to determine serum macromineral levels and trace elements in newborn calves with sepsis.

MATERIAL and METHODS

This study was conducted between 2010 and 2015 at the Large Animal Clinic, Faculty of Veterinary Medicine, Selcuk University. Five healthy and 25 calves with sepsis were used in the study. The calves were 2 to 35 days old and have different genders. Routine clinical examination of all the calves was performed. For diagnosis of sepsis, sick calves were examined in terms of parameters such as leucocytes count, body temperature, respiratory rate, suck reflex, dehydration degree, pulse, mental state, mucous membrane, capillary refill time and ability to standing. Laboratory and clinical findings as described by Aydogdu et al.[14] and Yıldız et al.[15] were used for the diagnosis of sepsis in the calves. For this purpose, calves with suspicious or present infection with SIRS criteria 2 and above were evaluated as sepsis.

Criteria for diagnosis of SIRS in calves were as follow; Leukopenia or leukocytosis (reference value, 4-12 10^3/µL), hypothermia and hyperthermia (reference value; 38.5-39.5ºC), bradycardia or tachycardia (<90 or >120 beats per minute), and tachypnea (>36 breaths per minute).

Blood sample for leucocytes count, macrominerals and trace elements analyses was collected from the *vena jugularis*. The tubes without anticoagulant were incubated at room temperature, and then their serum was removed by centrifugation for 5 min at 2500 g. Serum samples were stored at -20ºC until analyzed. Leucocyte levels in blood with K3EDTA of the calves were determined using a hematologic analyzer (Hemocell Counter MS4e, Melet Schloesing Laboratories, France). Sodium (Na), potassium (K) and ionized calcium (iCa) levels in heparinized blood were determined by a blood gas analyzer (GEM Premier Plus, Instrumentation Laboratory, Lexington, Mass). From the serum samples of the calves, calcium (Ca), boron (B), chromium (Cr), copper (Cu), iron (Fe), magnesium (Mg), phosphorus (P), sulfur (S) and zinc (Zn) concentrations were measured using inductively coupled plasma atomic emission spectrometry (ICP-AES, Vista model, Varian, Australia).

This study was approved by the ethics committee of Faculty of Veterinary Medicine, Selcuk University (Approval No: 2010/052).

Statistical Analysis

Kolmogorov-Smirnov test was performed to determine the normal distribution of data. Comparisons between the groups were made by conducting independent t test for variables with a normal distribution, whilst for variables that do not show normal distribution were analyzed with the Mann-Whitney U test. Data were presented as mean values and standard errors of mean (Mean±SEM) for variables with a normal distribution and median (minimum/maximum) values for variables that do not show normal distribution. The level of statistical significance was at $P < 0.05$. The SPSS software program (Version 18.0, SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

Hyperthermia or hypothermia, tachypnea, dehydration, tachycardia or bradycardia, depression, absence of sucking reflex, cooling in the extremities and in some cases, lateral recumbence were determined in calves with sepsis. In addition, capillary refill time (>2 sec) had been prolonged. Enteritis (n=18), pneumonia (n=4), intestinal obstruction (n=1), enteritis + arthritis (n=1), and pneumoenteritis (n=1) were diagnosed in calves with sepsis.

Differences in the clinical findings of sick and healthy calves are presented in *Table 1*. There was a significant increase ($P<0.05$) in respiratory rate and capillary refill

Table 1. *Clinical findings of calves with healthy and sepsis*

Parameters	Healthy Mean±SEM (n=5)	Sepsis Mean±SEM (n=25)	P Levels
Temperature (℃)	38.78±0.18	38.69±0.45	0.855
Pulse (min)	99.00±3.97	108.86±7.13	0.236
Respiratory rate (min)	34.40±3.92	60.43±6.94	**<0.001**
CRT (sec)	2.00±0.00	4.47±0.22	**<0.001**

CRT: Capillary refill time

time of the calves with sepsis compared with the control group. In addition, leukocytosis was observed in the calves with sepsis.

Macromineral and trace elements levels in sick and healthy calves are presented in *Table 2*. While blood Cu and K levels of the calves with sepsis were significantly higher (P<0.05), total Ca, iCa and Na levels were significantly lower (P<0.05) compared to the control group. Furthermore, compared to the control group, while blood Fe and Zn levels of the calves with sepsis were lower, the P and S levels were higher, no statistical difference was determined.

DISCUSSION

Due to its high morbidity and mortality, neonatal sepsis is one of the most significant health problems in cattle breeding [5,14,15]. The findings such as mild depression and losing suck reflex in the early period of sepsis are nonspecific. In sepsis, rectal temperature is variable (hypothermia or hyperthermia); however, a continuous tachycardia and even a tachypnea may develop. Furthermore, clinical symptoms related to hypotension and decreased cardiac output (prolonged capillary refill time, diminished peripheral pulses, cold extremities, decreased urine output) are evident and usually hypovolemia develops [1,4,15]. The findings for the diagnosis of sepsis according to observed hyperthermia/hypothermia, tachypnea, dehydration, tachycardia/bradycardia, depression, loss of sucking reflex, cold feeling in mouth, cooling down in extremities and in some cases, lateral recumbence, coma and prolonged capillary refill time used in this study are similar to clinical findings of sepsis *(Table 1)* stated in previous studies [1,4,14-19].

In human medicine, in sepsis and inflammatory diseases, the levels of trace elements, which have an important role in the continuation of cellular functions, stabilization of cell membranes, ensuring the efficacy of many antioxidant enzymes and the development of the immune response, and their efficacy are monitored and evaluated for prognosis and treatment [20-22]. In studies, it has been reported that in inflammation and sepsis, significant changes occur in the levels of blood copper and zinc [22-24]. Srinivas et al.[25], reported a decrease in blood Zn levels and an increase in Cu levels within a few days following infection in bacterially infected patients, and these changes persistand for weeks. An increase in serum Cu level and decrease in Zn level were determined in guinea pigs with intra-abdominal sepsis [22] and with experimental endotoxemic hamsters [26]. In studies of cattle with infectious bovine rhinotracheitis [27] and calves with diarrhea [11], a significant decrease in blood Zn level and a significant increase in copper level were determined. Endotoxemia causes negative mineral balance (hypoferremia and hypozincemia). Changes in mineral levels (such as iron and zinc) during the acute phase response help cleanse and protect the body from bacterial

Table 2. *Macromineral and trace element levels of calves with healthy and sepsis*

Parameters	Healthy n=5	Sepsis n=25	P Levels
Na (mmol/L) Mean±SEM	143.40±1.44	135.17±2.15	**0.004**
K (mmol/L) Mean±SEM	4.36±0.25	5.50±0.33	**0.013**
iCa (mmol/L) Mean±SEM	1.09±0.03	0.97±0.04	**0.031**
Ca (mg/L) Mean±SEM	136.21±2.50	119.85±3.14	**0.001**
B (mg/L) Median (min/max)	0.14 (0.10/0.23)	0.14 (0.07/0.59)	0.741
Cr (mg/L) Mean±SEM	0.06±0.01	0.06±0.01	0.805
Cu (mg/L) Mean±SEM	0.54±0.04	0.88±0.07	**<0.001**
Fe (mg/L) Mean±SEM	0.94±0.24	0.90±0.11	0.896
Mg (mg/L) Median (min/max)	69.57 (68.64/73.30)	68.23 (31.06/132.91)	0.487
P (mg/L) Median (min/max)	183.73 (177.28/194.26)	188.40 (139.36/545.15)	0.872
S (mg/L) Mean±SEM	520.35±27.89	558.95±24.95	0.323
Zn (mg/L) Mean±SEM	1.01±0.09	0.82±0.05	0.120

Na: sodium, K: potassium, iCa: ionized calcium, Ca: calcium, B: boron, Cr: chromium, Cu: copper, Fe: iron, Mg: magnesium, P: phosphorus, S: sulfur, Zn: zinc

invasion. On the contrary, an increase in blood copper level is usually seen in endotoxemia. This increase is accompanied by an increase in ceruloplasmin. Ceruloplasmin is an acute phase protein that increases from the initial stage of inflammation [1]. In this study, a significant increase in serum Cu concentration in the calves with sepsis *(Table 2)* but a decrease in Zn level compared to the control group were determined. It was considered that the increase in serum Cu level may be related to the increased level of ceruloplasmin (acute phase response), and the decrease in Zn level may originate from the increase of Zn transition from plasma to hepatocytes as a result of septicemia/ endotoxemia.

Hyponatremic, hyperkalemic metabolic acidosis is usually observed in dehydrated or endotoxemic neonatal ruminants [13]. Hyperkalemia is observed as a response to metabolic acidosis [28]. Functions of Na^+-K^+-ATPase pump at physiological pH limits are optimal. Inadequacy of Na^+-K^+-ATPase pump functions during acidemia begins and this causes an increase in intracellular Na and extracellular K ions [29]. In addition, impairment of renal K excretion associated with hypovolemia due to dehydration can also lead to hyperkalemia [30,31]. Hyponatremia is one of the common findings in the calves with diarrhea [13]. In this study, compared to the control group, a significant increase ($P<0.05$) in K level, and in contrast, a significant decrease ($P<0.05$) in Na level was determined in the calves with sepsis *(Table 2)*.

Serum calcium level can be affected by endotoxicosis. Total calcium concentration drops below 2 mmol/L in the cattle with experimental endotoxicosis [10]. Furthermore, hypocalcemia is one of the most frequently observed electrolyte abnormalities in intensive care units in human medicine. In 90% of critical patients, a low total calcium concentration is reported, and the prevalence of hypocalcemia, which is measured as ionized calcium is estimated to be 15-20% [32,33]. In addition, there was a relation between hypocalcemia and an increase in mortality of patients in intensive care units [33]. In this study, a significantly decrease ($P<0.05$) in both total and ionized calcium compared to the control group may be attributed to inadequate food intake or else to other factors which affect calcium absorption (SIRS, renal failure, insufficiency of Vit D etc.).

In conclusion, in this study, significant increase in K and Cu concentrations and significant decrease in Na and Ca concentrations were found in calves with sepsis. According to the results, K, Cu, Na and Ca may have an important role in the pathophysiology of sepsis. In addition, controlled studies to monitor changes in trace element and macromineral levels during the treatment of calves with sepsis would be beneficial.

Conflict of Interests

The authors reported that there was no conflict of interest.

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