Annals of R.S.C.B., ISSN: 1583-6258, Vol. 25, Issue 4, 2021, Pages. 20773-20777
Received 05 March 2021; Accepted 01 April 2021

evaluation of leptin serum changes in cases suffering systemic inflammatory response syndrome (SIRS) in dog

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ABSTRACT

Background and Objective: Systemic Inflammatory Response Syndrome (SIRS) is a complex set of events that may occur in animal cases because of an infectious or non-infectious cause. Therefore, the purpose of this study was to evaluate the serum changes of leptin in canine cases with systemic inflammatory response syndrome (SIRS).

Methods: The study was conducted as a prospective cross-sectional study. Of about 2500 cases admitted to the hospital, 37 canine cases admitted to the intensive care unit (ICU) were included in the study. To compare the results in the inpatient group with healthy dogs, 30 seemingly healthy dogs were selected as the healthy group and entered the study. During the study, in patient cases admitted to the ICU, hematological parameters, albumin and total protein were determined daily. Heart rate, temperature and respiratory rate were determined every 12 hours. Research data were processed in Excel and statistically evaluated in SPSS.

Results: The results showed that there was a direct relationship between increased leptin serum concentration and disease severity. There is an inverse correlation between disease severity and albumin. There is a direct correlation between disease severity and total protein. In many cases, monocytosis and neutrophilia occur. Serial and daily measurement of hematological and biochemical parameters to provide a better treatment strategy It is essential.

Conclusion: SIRS may lead to sepsis if it progresses. In such cases, the possibility of hypoalbuminemia is high. In the present study, the amount of albumin in dead dogs was significantly reduced compared to that cleared. This indicates an unfavorable prognosis of hypoalbuminemia in cases admitted to the ICU.

Keywords
Systemic Inflammatory Response Syndrome (SIRS), leptin serum changes, Canine Cases

Introduction

We were observing the establishment of several dog breeding centers in the country (Iran) given the expansion of the culture of keeping pets in recent years. One of the major challenges in veterinary hospitals now is the infectious diseases in puppies. In many cases admitted to the ICU, infection and sepsis lead to significant mortality. SIRS describes a clinical condition characterized by widespread activation of the inflammatory system, secondary to a sterile inflammatory disease or infectious bleeding. SIRS is associated with numerous diseases (like pancreatitis), trauma, burns, and major surgery and may not be associated with sepsis (1). It has to be noted that SIRS clinical signs differ in dogs and cats. The cats usually do not produce perdynamic responses (no red mucous membranes and no restrictive pulses) and are more likely to have relative bradycardia and hypothermia (2, 3). In one study, bradycardia was seen in 66% cats, highlighting the differences between dogs and cats in terms of their physiological responses to sepsis (2). SIRS has many clinical manifestations like the changes in body temperature, respiration rate, heart rate and leukocyte count.

Hematological and biochemical changes in small animals suffering from sepsis usually show the underlying disease's secondary underlying dysfunction in the organs. Moreover, probably hyperbilirubinemia may be secondary to cholestasis in dogs, and possibly in cats because of the loss of albumin from the body through the gastrointestinal tract or ulcers, diffusion into the third body space or permeability of arteries to the intercostal space, hepatic dysfunction and preferential synthesis of acute phase proteins by the liver. Ionized hypocalcemia is associated with prolonged hospitalization in both dogs and cats (5,6); there is hypoalbuminemia (4).

The animals suffering from SIRS or sepsis are initially hypercoagulable (hard to diagnose) but usually develop hypocoagulation due to the consumption of coagulation factors (7). When the immune system is fighting pathogns or repairing damaged tissue, proinflammatory cytokines signal immune cells such as T cells and macrophages to travel

to infection site. This production of "cytokine storm" and global activation of white blood cells (WBC) finally overshadows CARS and turns into a key in the pathognesis of SIRS. The diagnostic tools and prognosis of serum cytokine levels in the animals suffering from sepsis and SIRS is the subject of recent and ongoing studies (9, 8).

While no clinical findings for SIRS are pathognomic, the dogs with SIRS usually have some laboratory abnormalities. Complete blood cell counts usually indicate neutrophil leukocytosis with or without leftward deviation (10). Toxic changes in neutrophils are often seen with or without leukocytosis or leftward deviation. The biochemical tests may show blood sugar or hypoglycemia secondary to altered carbohydrate metabolism (10).

Timely intervention could enhance the outcomes in SIRS cases (11). After initiation, SIRS cannot be stopped immediately. Treatment includes addressing the underlying disease or cause and providing supportive care (11). The purpose is to prevent SIRS from progressing to MODS or MOF. Invasive fluid therapy is essential. If sepsis is suspected, antibiotic treatment should start immediately. Culturing potential sources of infection (blood and other body fluids) has to be done early so as not to delay the use of antibiotics (12). It is critical for the technicians to detect subtle changes in a case's vital signs quickly. Common monitoring involves evaluation of "upstream" macrovascular parameters like temperature, pulse, respiration, blood pressure, CVP and urine output (13). Given the points stated, acute sepsis and septic shock are the main challenges of the ICU in hospitalized cases. In spite of the significant advances in intensive care and emergency medicine, mortality from sepsis remains high. Thus, the purpose of the study was to evaluate the leptin serum changes in canine cases with SIRS.

Materials and methods

This study was conducted as prospective cross-sectional method. The dogs admitted to a private hospital over a period of 8 months were examined in the study. Out of about 2,500 cases admitted to the hospital, 37 sick dogs admitted to the ICU with three of the four conditions of tachycardia or bradycardia, tachypnea or bradypnea, leukopenia or leukocytosis, and fever or hypothermia were included in the study.

To compare the results in the inpatient group with the healthy ones, 30 seemingly healthy dogs with normal hematological results and no evidence of disease (heart rate, respiration rate and normal temperature) were selected as the healthy group (The age conditions of the healthy group was selected to be as similar as possible to the case group). All the dogs were examined during the study and were excluded in the event of premature death. A blood sample was taken from all dogs in the study when SIRS conditions were confirmed and transferred to two tubes containing EDTA anticoagulant and no anticoagulant. CBC was performed immediately and in case the CBC was normal and if there was no fever, they were excluded from the study and otherwise not.

The dog-specific ELISA kit was used to determine the value of leptin, and a Pars Azmoon kit made in Iran and a BT-2000 biochemistry analyzer were used to determine total protein and albumin. During the study, hematological parameters, albumin and total protein were determined on a daily basis in cases admitted to the ICU. Heart rate, temperature and respiration rate were determined every 12 hours. Data was processed in Excel software and statistically evaluated in SPSS.

Results

Thirty seven dogs admitted to the ICU of the hospital were selected for the study. Cases' age range was from 2 months to 11 years. Thirty healthy dogs with normal hematological results normal in terms of heart rate, respiration rate, temperature and health certification by a veterinarian were considered as the control group to evaluate the studied indices. The control group was selected similar to the case group in terms of age.

The mean serum leptin concentration in leukopenia dogs hospitalized in the ICU was 2.16 and ranged from 9 to 2.22 and the mean leptin serum concentration in leukocytosis dogs admitted to the ICU was 25.13 and ranged from 7 to 1.21. Serum leptin concentration in healthy dogs was 6.3. The results indicated a significant difference between the two groups ($p < 0.01$). Serum albumin concentrations were 2.5 and 2 in the hospitalized and healthy groups, respectively, with no significant differences between the groups. Although the total protein concentration in the hospitalized group increased compared to the healthy group, no statistically significant differences were found.

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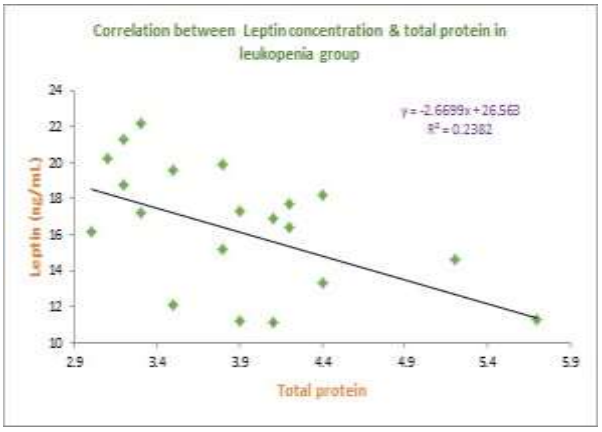
The hospitalized cases, according to the type of primary disease, showed that out of 37 cases, 29 were infectious, 2 genital, 1 gastrointestinal, 1 was renal, 2 tumor, 1 was cutaneous and 1 blood. Given the higher prevalence of infectious diseases in puppies, the majority of cases were under 6 months of age. Among the 37 hospitalized cases examined, 21 dogs had leukopenia at the time of admission and 15 had leukocytosis. Overall, 15 of the 37 hospitalized cases died during the study. Albumin was significantly reduced ($p < 0.05$) and protein levels were significantly increased in the cases who died compared to the discharged group. Albumin was an acute negative protein. Leptin significantly increased in the lost group compared to the cleared group ($p < 0.01$).

Moreover, it was found that high levels of leptin were directly associated with increased hospitalization time and the financial cost imposed on the livestock owner. There was a weak inverse correlation between albumin and leptin: albumin reduced significantly in the dead cases (Figure 1).

Figure 1: Correlation coefficient between albumin and leptin in leukopenic and leukocytosis dogs in ICU



A direct correlation is found between leptin and TP (Figure 2).

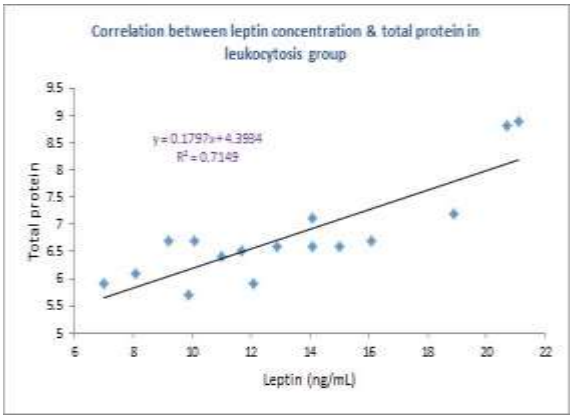


Figure 2: Correlation coefficient between leptin and total protein in dogs admitted to the ICU

Conclusion

Among the most important causes of SIRS in dogs are cancer, infection, heatstroke, acute pancreatitis, accident, autoimmune disease, peritonitis, burns and parvovirus infections. In the present study, in a period of 5 months, out of about 2500 cases admitted to the hospital, 37 cases with at least 2 conditions of SIRS were selected. In the present study, 1 case had gastrointestinal problems and mainly parvovirus puppies, 2 cases genital problems, 1 case renal disease, 1 case cutaneous, 1 case blood and 2 cases were cancer cases.

In the present study, 59% had leukopenia and 41% had leukocytosis. The results indicated that cases with lymphopenia have a worse prognosis compared to other cases. The study found a significant difference between leptin in hospitalized and healthy dogs. On the other hand, the higher the leptin, the higher the risk of death became. Thus, in the hospitalized cases died, leptin value significantly differef from the discharged group and one can state a significant relationship between leptin and increased mortality. The results showed that the albumin value in the control and case groups did not show much difference. This may be due to the case's condition. SIRS progresses to sepsis if it progresses. In such cases, the possibility of hypoalbuminemia is so high. In the present study, the albumin in dogs died significantly reduced compared to that discharged ones. This shows an unfavorable prognosis of hypoalbuminemia in cases admitted to the ICU.

Moreover, the albumin value in the group of gastrointestinal cases significantly increased compared to other groups. Lack of significant increase in total protein in the case group compared to the healthy group could be due to sampling time. Sampling was done at the start of the case's enrollment. As is seen in the serial measurements in the study, the value of total protein significantly increased in the second and third days of the study. No significant differences were found between healthy and sick groups at the beginning of the study. However, in the rest of the study and by examining the dead and discharged cases, a relationship was found between mortality and hypoglycemia. On the other hand, dextrose serum was used because of the continuous measurement of glucose in the inpatient ward, which maintained blood sugar levels during the treatment period in the present study.

Hematologic changes in the course of inflammation sometimes help and sometimes mislead. In the present study, all death cases had lymphopenia. Previous studies on the prognostic value of lymph nodes in critically ill dogs confirm this too. Neutropenia is one of the problems of cases admitted to the infectious ward. In the present study, 15 cases died. Overall, cases with neutropenia have a worse condition on the arrival and have a poor prognosis. Given the results of the study on a larger scale, measuring other indices that evaluate the status of inflammation and using the tests quickly diagnosing inflammation is suggested.

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