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C-Reactive Protein in Veterinary Practice

Yogeshpriya S* and Selvaraj P

Department of Veterinary Medicine, Tamilnadu Veterinary and Animal Sciences University, India

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***Corresponding author:** Yogeshpriya S, Department of Veterinary Medicine, Veterinary College and Research Institute, Orathanadu, Thanjavur-614625, Tamilnadu Veterinary and Animal Sciences University, India

Abstract

Animal body reacts to all kinds of injuries and stress to keep up the homeostasis mechanism of the body. This homeostasis achieved either by or nonspecific mechanism. The nonspecific innate resistance of the body like cytological and cytokine reactions including fever, leukocytosis etc. is known as acute phase response. In this response, there will be increase or decrease of serum concentration of proteins. These proteins are known as acute phase proteins. Measurements of serum concentration of these acute phase proteins are found to be useful in assessment of health status and prediction of diseases of the man and animals. The serum concentration of these acute phase proteins returns to base levels when the triggering factor is no longer present. The acute phase response is now considered to be a dynamic process involving systemic and metabolic changes providing an early nonspecific defence mechanism against insult before specific immunity is achieved. Use of one of the acute phase proteins, C-reactive protein as biomarkers for animal disease diagnosis and health status assessment has got high potential in modern veterinary practice is discussed in this review.

Keywords: Acute injury; C - reactive protein; Acute phase proteins; Veterinary practice

Abbreviations: CRP: C Reactive Protein; Hp: Haptoglobin; AGP: Acid Glycoprotein; SAA: Serum Amyloid A

Introduction

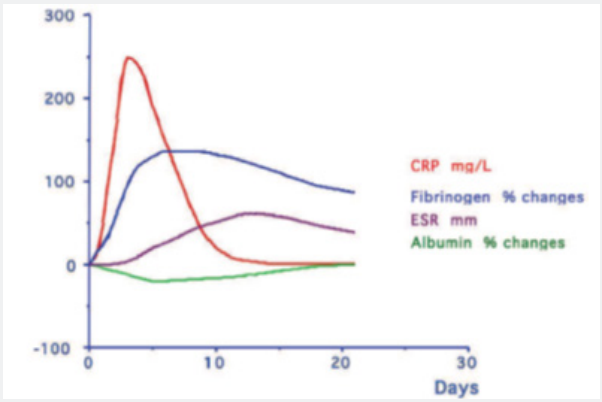

Figure 1: Changes in the CRP are the most rapid in response to inflammation when compared to fibrinogen, Erythrocyte sedimentation Rate and Albumin.
(Source: Associate Professor Lars-Olof Hansson, Karolonska Hospital, Sweden)

The acute phase reaction encompasses all the phenomena which take place in animals following tissue damage and is particularly associated with inflammation from whatever cause. During the acute phase reaction, the body mounts a multifactorial response to remove and replace damaged tissue and one of the mechanisms involved is the production and secretion by the liver of a number of 'acute phase proteins' [1]. The concentrations of these proteins increase during the reaction are called as Positive acute phase proteins (APPs) such as C reactive protein (CRP), Serum Amyloid A (SAA), Haptoglobin (Hp), Ceruloplasmin, α2- Macroglobulin, α1 Acid Glycoprotein(AGP), Fibrinogen and Complement (C3,C4) while those of others, including albumin, Transferrin, Transthyretin and Retinol-binding protein decrease as the liver switches production of protein towards the synthesis of the proteins required to deal with the damage; is called as negative APPs [2] (Figure 1).

Biological functions of C-reactive Protein

The protein was named the C-reactive protein because of its ability to bind pneumococcal C-polysaccharide. The presence of CRP has also been described in human patients during acute infections caused by acute lobar pneumonia, active rheumatic fever and bacteraemia caused by "colon bacillus". Among the biological functions described in the literature are Complement activation and opsonisation [3,4] Modulation of monocytes and macrophages, cytokine production [5] Binding of chromatin [6] Prevention of tissue migration of neutrophils.

CRP in Bovines

During the early stages of infection, the serum concentration of CRP increases [3]. This increase has been described to be evident before an elevated rectal temperature is observed. Even

though increased concentrations of bovine CRP during naturally occurring infections and a correlation with herd health status have been reported, CRP is generally not considered an acute phase protein in cattle. As stress increases to a critical point, the liver rapidly synthesizes large amounts of CRP and releases it into the blood to provide immediate protection against stress [7]. Diseases in a dairy herd elevated the serum CRP level. The serum CRP level was also correlated with milk production. The greater the milk production, the higher the level of serum CRP. Diseases, especially acute infections, induced much higher levels of CRP production than stress or lactation. Also showing that plasma C-reactive protein concentration is related to different kind of stress (poor health, high lactation, blood collection). Strong correlation was observed in cows after delivery (0-1 month) between fibrinogen and CRP values [8]. Obtained results suggest that not only inflammations but also physiological factors such as pregnancy, delivery and/or state of lactation may have a significant impact on APPs values in the blood plasma of dairy cows. It would be worth in the future to check whether there is a relationship assessing the animal health status obtained using acute phase proteins method relatively to other indicators, such as milk yield, length of lactation or others. Morimatsu [9] also discovered Elevation of bovine serum C-reactive protein by lactation when compared to other Acute Phase protein such as serum amyloid P component levels (Figure 2).

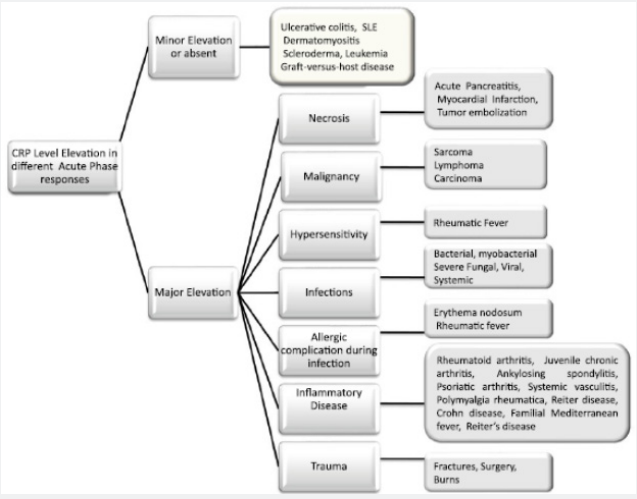

Figure 2: CRP in different types of acute-phase response and disease (Source: Waliza Ansar and Shyamasree Ghosh).

CRP in Swine

In the pigs, as in the dogs and humans, C-reactive protein (CRP) is the prototypical acute phase protein with major diagnostic value. CRP concentrations are useful for evaluating the health status of a swine herd, but not for the health status of an individual animal or the differentiation of diseases. Serum haptoglobin (HP) concentration is better than serum CRP concentration as an indicator of inflammatory reactions in pigs, and HP is an important marker for swine health status [10]. On the other side, pigs undergone experimental study had CRP serum concentration below 22µg/ml (mean 18.64 ± 2.59). Twenty-four hour after coinfection with swine influenza virus (H1N1) and Pasteurella multocida, the mean concentration of CRP reached 62.85 ± 35.55µg/ml. Significant difference were noticed as compared to control animals [11]. The presence of elevated serum Hp and CRP concentrations in apparently healthy pigs at slaughter could provide important information to a veterinary inspector about the presence of sub-clinical lesions that could lead to condemnations or a decrease in the quality of carcasses [12].

CRP in Canines

In canines CRP is the major APP used as marker for systemic inflammation / infection. Normally the level of CRP is less than 1.5 mg/ dL or even lower than 0.5 mg/dl. The normal range may be 0.08 to 2.26 mg/dl [13]. The level rises within 4 to 6 hrs after onset of inflammation / infection. Serum CRP level above 3.5 mg/dl, indicates presence of systemic inflammation. Level above 5 mg/dl is a strong evidence of systemic inflammation. Strong correlation was observed between CRP and animal's temperature and Total Leukocyte counts of canine patients naturally infected with Leptosporosis [14]. CRP levels could be used to monitor early responses to antibiotic treatment and might alert veterinarians to the need for further evaluation or additional treatment. Serum CRP concentrations provide useful information about the severity of inflammation inside the Urinary Bladder. These correlations suggest that CRP concentrations can represent a safe, convenient, and alternative method for evaluating the status of bacterial cystitis [15]. Significantly high CRP values were observed in cases like Lympoma, pyometra, panniculitis, acute pancreatitis, polyarthritis, leptospirosis, babesiosis, parvo viral enteritis, glomerulonephritis, immune mediated disease and malignant neoplasia [16]. Rise in CRP may not be observed in local tumours like leiomyosarcoma, upper respiratory tract infection, diabetes, neurological problems involving intracranial disorders. Since the CRP concentration did not increase in patients with intervertebral disk protrusion, it might be useful in distinguishing arthritis from spinal / brain diseases in patients with lameness. Thus, CRP is a nonspecific inflammatory marker, it could facilitate the diagnosis by indicating the presence and the extent of inflammation.

CRP in Elephants

The reference interval for CRP reported herein for Asian elephants (1.3–12.8 mg/l) is like CRP intervals reported in harbor seals (*Phoca vitulina*) and bottlenose dolphins (*Tursiops truncatus*). When compare to the CRP, SAA is demonstrated to be the most responsive major APP in elephants [17]. This agrees with previous reports where SAA elevations were noted consistently in elephants with Elephant endotheliotropic herpesvirus (EEHV) and in 2 captive elephants with inflammatory lesions. Further studies are needed to address the reactivity of the CRP reagents with elephant proteins and to consider the use of either elephant-specific reagents or non–antibody-based assays.

CRP in Chicken

The birds positive for *E.Coli*, *Pasturella multocida* and *Staphylococcus aureus* infections as well as histomoniasis and

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adjuvant injection found to be positive for CRP. CRP also positive in clinically normal population. These birds on post-mortem, had lesions consistent with chronic respiratory disease, which is highlighting the use of CRP as a potential biomarker for non-clinical disease [18]. CRP did not rise in chickens as quickly as it does in humans, whereby CRP was detectable 36-48 hours post infection in chickens, compared to 16-18 hours in humans. A more recent study investigated CRP serum concentrations using a human CRP kit and found CRP concentrations to increase.

CRP in Equines

A high serum concentration was also found in horses with pneumonia, enteritis, arthritis and after castration. Increased plasma concentration has been observed in carbohydrate induced laminitis. Increased serum concentration of CRP has been found in horses suffering from aseptic inflammation induced by intramuscular turpentine injections [3].

Conflict of Interest

The authors declare no conflict of interest.

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