Review Article

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BACTERIAL RESPIRATORY DISEASE OF CATTLES

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ABSTRACT

Bovine Respiratory Disease Complex (BRDC) is one of the most important diseases in all over the world. It affects the lower respiratory tract and is responsible for economic losses due to mortality, treatment costs. BRDC has a multifactorial factors such as infectious agents, host, and age, breed, genetic, nutrition, climate, commingling of animals and especially crowded transport. Especially transportation has a close relationship with an increased risk of BRDC because it is responsible to weaken immune system. Therefore, Mannheimia haemolytica, Pasteurella multocida, Histophilus somni, Mycoplasma bovis, and Bibersteinia trehalosi are most common BRDC pathogens that are still tried to develop diagnostic techniques and control strategies. In addition, good nutrition, vaccination and reducing stress factors, complying with biosafety rules and ensuring adequate air circulation are important factors in the control of respiratory system disease in cattles.

INTRODUCTION

Bovine Respiratory Disease Complex (BRDC), is a significant health problem for all types and all ages of cattle in the dairy and livestock industry. However, the availability and use of numerous vaccines against bovine respiratory pathogens and newer antibiotics, and an improved understanding of the etiology of BRDC, from pneumonia to death, it remains a major cause of morbidity, mortality and economic losses in industries. Also, BRDC treatment is a significant expense for producers, with annual BRD costs in the United States estimated at 800-900 million dolar[1,2].

Respiratory disease usually occurs within 6 to 10 days after multiple stress factors such as shipping or commingling, with interstitial pneumonias often occurring 70 or more days later[3]. Multiple factors such as predisposing, environmental, and epidemiological can cause of BRDC. Especially epidemiological factors that several studies represented the bacterial pathogens as *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, *Mycoplasma bovis*, and *Bibersteinia trehalosi*[4,5]. Firstly, researcher presented BRD complex pathogens only *Mannheimia haemolytica* (formerly *Pasteurella haemolytica*), and *Pasteurella multocida* since then, *Histophilus somni* (formerly *Haemophilus somnus*), *Mycoplasma bovis*, and, most recently, *Bibersteinia trehalosi* (formerly *Pasteurella trehalosi*) have also been recognized as additional bacterial agents associated with severe bovine bacterial pneumonia. These bacteria are saprophytic in the respiratory tract of animals, but under stressful conditions (e.g., weaning, transport, or stress) and may become pathogenic and cause BRDC4. BRDC can occur in every age of cattles, including feedlot, dairy calves, nursing beef, post-weaned [6,7]. The role of BRD in morbidity and mortality rates may range 35-100%, 24-60% have been reported

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respectively in several studies[8]. Antibiotics is the key of treatment and 89% of sick cattle are treated but 33% of the cases, the treatment fails, resulting in additional treatment is required or animal death[9]. In this review we will focus on pathogenic bacterias in BRDC and how the these pathogens develops pneumonia phenomonia.

A. Major BRDC Pathogenic Bacteria

1. *Pasteurella* spp.: *Pasteurella multocida* (*P. multocida*) is a pathogenic, Gram mnegative coccobacillary- to rod- shaped microorganism that belongs to the genus Pasteurellaceae. It is often found as normal oropharyngeal flora in animals and it can also be primary or opportunistic pathogen[10-11].

P. multocida is divided into three subspecies, five capsular serogroups and 16 serotypes. Especially *P. multocida* serogroup A isolates are both bovine nasopharyngeal commensal, and pathogen for young dairy calves and cattles. This pathogen can be main component of Bovine Respiratory Disease Complex (BRDC), enzootic calf pneumonia and shipping fever of weaned, stressed animals[11-13]. *P. multocida*-induced pneumonia is associated with predispose factors such as environmental, epidemiological and stress factors (shipping, co-mingling, and overcrowding). Lung lesions of infected animals are characterized as an acute and subacute bronchopneumonia with pleuritis or without[14]. After proper clinical examination of the cattles suffered with septisemic or systemic pasteurellosis, animals shows clinical signs of increased body temperature, loss of appetite, depression, excessive salivation, edema of the head, neck, and brisket, and severe respiratory distress with foamy nasal discharge, leading to death. Acute form of septicemic pasteurellosis death will occur in less than 24 h. However 100% of all mortality rates are associated with acute sepsis manifest, treatment with antibiotics is possible in the early stages [11,15].

2. *Mannheimia* spp.: *Mannheimia haemolytica* (*M. haemolytica*) is Gram negative, coccobacillary- to rod- shaped bacteria that previously belonged to the Pasteurellaceae family. *M. haemolytica* causes Mannheimiosis, shipping fever and pneumonic pasteurellosis tahta are most common respiratory diseases of cattles and is responsible for approximately 30% of all cattle deaths worldwide. It has been reported that of the 12 capsular serotypes of *M. haemolytica*, A1 and A2 are common all over the world and both colonize the upper respiratory tract of cattle and sheep[16]. Although other serotypes such as A6, A7, A9 and A12 have been reported in the etiology of the disease, A1 is considered the most important cause of bovine mannheimiosis. Studies have reported that serotype 1 is found at a rate of 70.7% in individuals with respiratory system disease[17,19]. *M. haemolytica* occurs as part of the commensal nasopharyngeal microflora in healthy animals and can control the growth of bacteria in the nasopharynx. Also, few bacteria inhaled in aerosolized droplets are cleared by the host immune system. In stressed animals, *M. haemolytica* A1 can proliferate and reach high numbers in the nasopharynx and trachea, causing large numbers of bacteria to be inhaled and colonized in the lungs[16-19]. As known from Pasteurellosis, healthy animals are at risk in an enclosed environment during transport, under stress within the other conditions, this situaton is similar in *Mannheimia* infections[19].

3. *Histophilus somni*: *Haemophilus* spp. is pleomorphic, Gram negative rods or coccobacilli and obligate inhabitants of animals. *Histophilus somni* (formerly *Haemophilus somnus*) is "blood-loving," because blood or blood factors were originally required to isolate these bacteria. Also nicotinamide adenine dinucleotide (NAD or NAD phosphate; V factor) or protoporphyrin IX or protoheme compounds such as hemin (X factor) or both are crucial for growing[20-23]. It is a complex disease in cattle characterized by septicemia, thrombo-embolic meningoencephalitis, polysyonivitis, fibrinous pluritis, myocarditis, otitis media, infertility, reproductive disorders, mastitis and suppurative bronchopneumonia. Among them, the system or tissue most affected is the lung parenchyma. Therefore, it is considered one of the most important bacterial agents of acute and chronic BRDC[22]. It can cause fibrinous bronchopneumonia with or without other respiratory pathogens. Severe consolidated areas occur in the lungs in cases of acute pneumonia due to *H. somni*. Interstitial pneumonia, characterized by infarct areas as a result of hemorrhage, thrombosis, occurs. Severe laryngitis and hemorrhagic tracheitis often accompany pneumonia in these animals. *H. somni* cannot survive long periods in the environment, colonize new hosts and transport by direct contact, asymptomatic carrier, contaminated fomites and inhalation[22-24].

4. *Mycoplasma bovis*: Mycoplasmas are one of the two genera of the family Mycoplasmataceae, one of the three families of the class Mollicutes and are unique procaryotes that lack a cell wall and have the smallest cell size microorganisms.

Mycoplasmas require the addition of animal protein, sterol component and DNA source to the medium. Typical colony structure appears as 'scrambled eggs' on the surface and deep into the agar[25,26].

Clinically healthy animals can carry the agent in the mucosa of the nose, conjunctiva, mouth, intestine and genital tract without showing any signs. Respiratory problem, including pneumonia and pleuropneumonia, is the most common clinical manifestation of mycoplasmas in mammals and also arthritis, and tenosynovitis clinical signs in feedlot cattle. The agent is mainly located in the bronchoalveolar region in the respiratory tract and spreads to the environment in the form of cough and droplet infection[27,28]. Contaminated dust particles can also be a source of infection. Following the development of infection in the respiratory system, the disease spreads rapidly in the herd. The agent is found in the nasal discharge of animals within 24 hours following contact with a diseased calf. One week after the initial detection of the agent, *M. bovis* can be isolated from most animals in the herd. Depending on various stress factors, mycoplasmosis may form 7-14 days after the development of BRDC or shipping fever. *M. bovis* causes a variety of respiratory symptoms, but they are not ethiological specific; fever, loss of appetite, depression, hyperventilation, dyspnea, fever and can occur even in five day old young calves[29-31].

B. Pneumonia Types of BRDC

Suppurative Bronchopneumonia (Lobular Bronchopneumonia)

Suppurative bronchopneumonia is common type of pneumonia of young dairy calves, and it is most often related with *P multocida* infection. This is characterized bilateral and localization of the cranioventral lobes and presents with mucopurulent exudate flow of different color and consistency from the cross-section of the organ[14,32,33]. This type of pneumonia is mostly in the form of lobular consolidation and is therefore also called lobular pneumonia. Depending on the type of pathogen and the duration of the fire, the macroscopic image of the lung takes different forms. Generally, the lungs are hyperemic and edematous within the first 12 hours. After approximately 48 hours, consolidation and a hard consistency occur as neutrophils infiltrate the area. The hyperemic image disappears within 3-5 days and a gray-pink image occurs. In bronchopneumonias, the lungs are seen macroscopically as flesh-colored and viscous; lesions are in the form of patches. Because of the exudate filling into the air spaces, the pieces taken from the lung do not float when thrown into the detection fluid[14,32-34].

Fibrinous Pneumonia or Fibrinous Pleuropneumonia (Fibrinous Bronchopneumonia, Lobar Pneumonia)

Fibrinous bronchopneumonia is typical of that produced by *M haemolytica* and to a lesser extent *H somni* and is the most common form of acute pneumonia in weaned, stressed beef cattle (shipping fever). The inflammation spreads rapidly until it covers the entire lobe. In general, fibrinous bronchopneumonia occurs in more severe lung injuries and is more severe, causing death of the animal. Clinical signs and death occur as a result of severe toxemia in approximately 30% of events. As with suppurative pneumonia, there are initially red areas of consolidation. After about 24 hours, the interlobular septum enlarges with edema and fibrin outflow; Thrombosis is seen in arterioles, venules and lymphatic vessels. Lung lobes take a marble appearance macroscopically[32-34].

Caseonecrotic Bronchopneumonia:

Chronic Mycoplasma infection especially caused by *M bovis* pneumonia type is caseonecrotic bronchopneumonia. Cranial and medial lung lobes are more affected in caseonecrotic bronchopneumia. Nodules containing caseous necrosis are found in the affected areas of the lung, often with consolidated lung tissue adjacent to these areas. Caseonecrotic nodules can range in size from mm-cm[35-36]. Generally, nodules of this type are circular, white, dry and easily fragmented nodular lesions that protrude from the pleural surface. Caseous lesions are sequestered over time and can spread to the entire lobe and form bronchiectasis. Especially in cases where coinfection with other BRDC bacteria occurs, these areas of caseous necrosis may become a liquid, pus-filled structure instead of dry fissile material[37,38].

C. BRDC Prevention and Treatment Strategies

Vaccination: Vaccination of the cattles against to respiratory bacterial infection to enhance immunity by increasing antibody concentration and it has been proven for dissemination of the immunity39. At the same time, the scientific community continued to develop and innovate diverse and complex vaccine designs to activate various arms of the immune system and combat pathogens virulence mechanisms such as modified-live viral vaccines (MLV), killed virus (KV) vaccines or a combination of BRD-associated bacteria bacterin/toxoids that are commercially available against BRD-associated viruses and bacteria[40]. Especially for beef cattles, studies highlighted that vaccination of calves against to Mannheimia haemolytica/Pasteurella multocida, may reduce the incidence of morbidity and mortality41. Interestingly, some researchers claimed that vaccination efficacy against *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* is inconsistent[42].

Antibiotic terapy: In the feedlot industry, the use of antibiotic therapy represents a vital management activity to control and treat BRD[43, 44]. Generally, third-generation ceftiofur and fourth-generation cefquinom are most commonly prefered in the treatment and florfenicol, oxytetracycline, tilmicosin, tulathromycin, chlortetracycline and chlortetracycline plus sulfamethazine are used for metaphylaxis in the feedlots[43,44]. Also it should be noted that, after using long-acting oxytetracyclines if there is no sign of improvement in 5-10% of the sick animals within the first 24 hours, the treatment should be continued with tilmicosin or florfenicol. Antibacterial choices for treatment may be diverse for cattles. Sulfonamides are not the first drugs to be considered in the treatment of severe respiratory system infections. They show a bactericidal effect by preventing the formation of the cell wall in bacteria. Due to their mechanism of action and spectrum, they are mostly preferred in acute events and upper respiratory tract infections. Also erythromycin, tylosin and gamithromycin are used in the treatment due to their ability to accumulate in the respiratory system at high concentrations. Fluoroquinolones show synergistic activity with beta-lactams, and antagonist activity with macrolides and phenicols. Although enrofloxacin and ciprofloxacin are well known antibiotics, danofloxacin penetrates lung tissue better than enrofloxacin; veterinarians has given priority for this reason[43-45].

Biosecurity: Biosecurity in cattle breeding covers a series of measures taken to prevent the transmission of epidemic disease factors to animal herds at the enterprise, regional or national level. The term biosecurity is particularly relevant to the protection and safety of dairy cattle against respiratory diseases[46]. Biosecurity consist important routine applications such as farm management, daily care, feeding, health controls[47]. Measures to be implemented to protect both animals and employees in the enterprise include biosecurity-based practices that prevent the pathogen from entering the herd46. These practices are part of the often recommended measures to control many infectious diseases, as they reduce the risk of disease spreading. The producers and veterinarians should be carried out the biosecurity management more rigorously applied for the reduction of respiratory disease prevalence in cattle, including (1) strategic vaccination, (2) calf biosecurity, (3) housing ventilation, (4) commingling and animal contact, and (5) virus control[46].

CONCLUSION

As a result of all this detailed evaluation of BRDC, precautions must be taken on biosecurity practices, production management strategies for minimizing pathogen shedding, exposure, and transmission respiratory disease in cattles. In addition good nutrition, vaccination and reducing stress factors, complying with biosafety rules and ensuring adequate air circulation were important factors in the control of respiratory system disease in cattles. Various combinations of these control measures should be adapted to individual farms to help decrease the morbidity and mortality attributed to respiratory disease.

Conflict of interest statement

The authors declare that they have no conflicts of interests.

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