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Bovine Respiratory Disease Complex – A Review

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Bovine respiratory disease (BRD) complex is a respiratory syndrome caused by various infectious agents and represents a major economic and health problem in bovine population worldwide. Stress is the probable predisposing factor for the development of BRD complex in bovines worldwide and is also a disease of economic importance to the bovine industry. One of the challenges of bovine respiratory medicine is early detection of clinical cases of BRD. This is especially important in subclinical forms of the disease, which can be easily missed and cause important economic losses. Also, the preventative approaches to the disease are not enough. In this article, basic characteristics and current diagnosis, treatment and prevention approaches of BRD were reviewed.

Introduction

Many of the diseases that have been shown to impact the respiratory tract of cattle have been grouped into an overall category known as bovine respiratory disease (BRD) complex. This includes shipping fever syndrome, mucosal disease, enzootic calf pneumonia, acute respiratory distress syndrome, hemorrhagic syndrome and atypical interstitial pneumonia (Baker, 1995; Ames, 1997; Apley, 2006). Bovine respiratory disease is a result of the complex interaction of bacterial and viral agents, environmental conditions, management factors and the animal health (Yates, 1982; Mcvey, 2009; Nickell and White, 2010). It is a major health problem of respiratory system occurring worldwide in both dairy and feedlot cattle (Edwards, 2010), responsible for high morbidity and mortality and has been reported to cause heavy economic losses in terms of drug and veterinary costs, extra labour and production losses (Van der Fels-Klerx *et al.*, 2001; Gagea *et al.*, 2006; Abutarbush *et al.*, 2012). The disease is estimated to cost $800 million–$1 billion annually in the USA (USDA/Agriculture Research Service, 2011), but there is no report regarding the economic loss in India due to BRD complex. The clinical signs of BRD complex vary according to the animal status, the level of stress that animal experiences, management practices and quantum of pathogen challenge (Sanderson, 2008; Smith, 2009; Snowder, 2009).

Predisposing factors

Animal health status is characterized by the balance between protective factors (animal resistance) and risk factors (Leblanc, 2006; Taylor, 2010). This balance depends on the interaction among the susceptible host, etiologic pathogens and the environment. Stressful managemental practices (e.g. weaning, castration, transportation, commingling, etc.) promote the transmission and proliferation of commensal, but potentially pathogenic, microbes situated in the upper respiratory tract of healthy cattle (Apley, 2006; Confer, 2009; Griffin *et al.*, 2010). Viral and bacterial agents proliferate, become pathogenic and damage the respiratory tract during the progression of subsequent respiratory disease (Griffin *et al.*, 2010; Panciera, 2010).

Etiology

Viruses play an important role in the development of BRD complex since they predispose the animal's lung parenchyma to bacterial infection by causing direct damage to the respiratory mucosa and inhibit the animal's defense mechanism against bacteria that are commensal in the upper respiratory tract (Hogdson *et al.*, 2005; Taylor, 2010). The major viruses involved in precipitating this disease complex are bovine herpesvirus-1 (BHV-1) leading to Infectious Bovine Rinotracheitis (Hage *et al.,* 1998), parainfluenza virus-3 (PIV-3) (Hartel *et al.*, 2004), bovine respiratory syncytial virus (BRSV) (Elvander, 1996) and bovine viral diarrhoea virus (BVDV) (Van Reeth and Adair, 1997). Bovine viral diarrhea virus has been recognized as a major pathogenic partner associated in the development of BRD complex (Griffin *et al.,* 2010; Panciera, 2010). In addition, bovine respiratory coronavirus, adenovirus and influenza-A virus have also been identified as viral pathogens involved in the development of BRD complex (Gay and Barnouin, 2009). Bacterial pathogens involved in the development of BRD complex include *Pasteurella multocida*, *Mannheimia haemolytica* (formerly *Pasteurella haemolytica*), *Histophilus somni* (formerly *Haemophillus somnus*) and *Mycoplasma bovis*(Confer, 2009; Griffin *et al.*, 2010, Grisett *et al.*, 2015). Other bacterial pathogens associated with BRD complex include *Arcanobacterium pyogenes*, *Bibersteinia trehalosi* and other species of *Pasteurella* and *Mycoplasma* (Griffin *et al.,* 2010).

Diagnosis

The clinical diagnosis of BRD complex is classically based on characteristic clinical signs and symptoms (Buczinski *et al.*, 2014). These signs which are used to make a diagnosis of respiratory disease of calves are fever, cough, ocular or nasal discharge, abnormal breathing, and auscultation of abnormal lung sounds (McGuirk and Peek, 2014). Different practical tools have been developed by researchers and producers for both beef and dairy calves (Buczinski *et al.*, 2014). Love *et al.*, (2014) developed clinical scoring systems for BRD complex. There are some different clinical scoring systems for BRD. The first system values are coughing (induced or spontaneous coughing, 2 points), nasal discharge (any discharge, 3 points), ocular discharge (any discharge, 2 points), ear and head carriage (ear droop or head tilt, 5 points), fever (≥39.2 °C or 102.5 °F, 2 points), and respiratory quality (abnormal respiration, 2 points). Calves are categorized "BRD positive" if their total score is ≥4. This system correctly classified 95.4% of positive cases and 88.6% of controls. The second presented system categorized the predictors and assigned weights as follows: coughing (spontaneously, 2 points), mild nasal discharge (unilateral, serous or watery discharge, 3 points), moderate to severe nasal discharge (bilateral, cloudy, mucoid, mucopurulent, or copious discharge, 5 points), ocular discharge (any discharge, 1 point), ear and head carriage (ear droop or head tilt, 5 points), fever (≥39.2 °C, 2 points), and respiratory quality (abnormal respiration, 2 points). Calves were categorized "BRD positive" if their total score is ≥4. This system correctly classified 89.3% of positive cases and 92.8% of controls. The third presented system using the following predictors and scores: coughing (spontaneous only, 2 points), nasal discharge (any, 4 points), ocular discharge (any, 2 points), ear and head carriage (ear droop or head tilt, 5 points), fever (≥39.2 °C, 2 points), and respiratory quality (abnormal respiration, 2 points). Calves are categorized "BRD positive" if their total score is ≥5. This system correctly classified 89.4% of positive cases and 90.8% of controls. Each of the proposed systems offers few levels of clinical signs and data-based weights for on-farm diagnosis of BRD in dairy calves (Love *et al.,* 2014).

Whole blood and nasal swab samples, nasopharyngeal swab and bronchoalveolar lavage fluid can use for detection of BRD agents with PCR and ELISA techniques (Klima *et al.,* 2014; Capik *et al.,* 2017; Rodriguez-Castillo *et al.,* 2017). But periodical monitoring of the infectious agents is not practical, also expensive for a lot of farm. To improve diagnostic accuracy, several authors have focused on ancillary tests using various blood biomarkers. For example, the acute-phase proteins (APP) change in concentration after infection, inflammation, surgical trauma, or stress and can either increase (positive APP) or decrease (negative APP) as a consequence of inflammatory stimuli before the clinical signs. Haptoglobin (Hp), serum amyloid A (SAA), and fibrinogen (Fb) are among the most commonly reported APPs. The C-reactive protein (CRP) has also been mentioned in various species (eg, human or dog) as an important APP but has received limited interest in cattle. The serum increase of APPs can occur as soon as 4 hours after the insult for SAA and CRP or later (24-48 hours) for Hp and Fb (Abdallah *et al.,* 2016). Antigen of some virus species, such as BVDV, BHV-1, PIV-3 or BRSV can also be identified using isolation test or ELISA methods (Uttenthal *et al.,* 1996; Autio *et al.,* 2007). Molecular biology techniques have also been employed to identify the viruses species-specific PCR and rt-PCR methods (Autio *et al.,* 2007). Along with these methods some new diagnostic techniques are used now a days for the detection of BRD complex such as Virus neutralization test, Immunohistochemistry, *In-situ* hybridization, Complementary fixation test (CFT), Agglutination test, Antigen capture ELISA and multiplex PCR (Fulton and Confer, 2012; Jamali *et al.,* 2014).

Important haematological findings associated with BRD complex include leokocytosis, neutrophilia, increased fibrinogen concentration and acute phase proteins. The availability of a rapid test for acute phase proteins could assist in the field diagnosis of the disease and its possible differentiation from similar diseases (Radostits *et al.*, 2007, Richeson *et al.*, 2013). Biochemistry in BRD complex reveals lower serum phosphorous, magnesium, potassium, iron and alkaline phosphatase levels and higher bilirubin and aspartate aminotransferase levels in affected animals (Martin and Lumbsden, 1987).

Control and metaphylaxis

As the disease is responsible for high morbidity and mortality causing heavy economic losses to the farmers, its timely diagnosis and treatment is very essential. Various antimicrobials have been tested and used with variable efficacy for therapeutic purpose in BRD complex from time to time. Commonly used antimicrobial drugs are penicillin (Mechor *et al.*, 1988), enrofloxacin (Hamm *et al.*, 1999), oxytetracycline (Keita *et al.*, 2007), ceftiofur sodium (Hibbard *et al.*, 2002), levofloxacin (Dumka and Srivastava, 2006), florfenicol, tulathromycin (Perrett *et al.*, 2008, Arslan *et al.*, 2010), marbofloxacin (Grandemange *et al.*, 2012) and clinafloxacin (Sweeney *et al.*, 2013).

Unfortunately, routine screening of calves for respiratory disease on the farm is rarely performed (McGuirk and Peek, 2014). The vaccines available to prevent BRD continue to improve (Hilton, 2014). In addition, a nitric oxide releasing solution (NORS) has been developed and shown to have potential in the prevention of BRD (Sheridan *et al*., 2016). In the other hand, purchasing single-source cattle which known history of pre- and post-weaning procedures can minimize pathogen exposure and enhance immunity. Using cattle-handling techniques and facilities that promote low stress will allow host immune defences to remain effective against bacterial and viral colonization. Also, controlling BRD must be managed through a comprehensive herd health immunization and management program that effectively addresses disease challenges common to the operation (Lee *et al.*, 2005; Edward, 2010)

In conclusion, BRD complex is still an important topic and seems to will be serious problem for cattle industry in future time because of its complex nature of etiological agents, difficulties of early diagnostic and treatment situations. Improving antibiotic resistance of the pathogens is one of the negative parts of the situation; therefore treatment alternatives are getting decrease. In this frame, prevention and early diagnose of BRD complex have more importance for future of the cattle industry worldwide.

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