Human and animal brucellosis: Literature review

Brucelose humana e animal: Revisão de literatura

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Keywords: Brucellosis, Public health, Clinical manifestations.

1 INTRODUCTION

Brucellosis is caused by Gram-negative and facultative intracellular bacteria of the genus *Brucella*, being a zoonosis of wide distribution and worldwide significance, whose incidence and prevalence vary according to the country (DE SOUZA *et al*., 2009; SOLA *et al.*, 2014). Worldwide, about 500,000 new cases of human brucellosis are reported annually (WU *et al*., 2022).

In addition to humans, brucellosis affects several species of mammals, being considered as a debilitating disease (LAWINSKY *et al*., 2010) with several clinical manifestations, with a predominance of reproductive changes (RODRIGUES *et al*., 2017; SILVEIRA et *al.*, 2015), which causes great economic repercussions, due to losses due to infertility, abortion and drop in milk production (DADAR *et al*., 2019).

In humans, it can be caused by *B. melitensis*, B. *abortus*, *B. suis* and *B. canis* species (LAWINSKY *et al.*, 2010). In dogs, the disease is usually associated with *B. canis*, which can penetrate through mucous membranes, mainly oral, genital and conjunctival (RODRIGUES *et al*., 2017). In cattle, brucellosis is caused by *B. abortus*, whose presence in herds can cause economic losses and public health risks (BATAIER NETO *et al*., 2009; PACHECO *et al.*, 2008), since humans can be affected by contact with aborted fetuses, fetal wrappings, placental remains and blood from infected animals, or by consuming *fresh* milk and its derivatives.

Among the most prevalent reproductive changes in cattle, abortion in females stands out, especially in the final third of pregnancy, while bulls can develop orchitis and

epididymitis (BATAIER NETO *et al*., 2009). *Ovine* brucellosis caused by *B. ovis* is characterized by epididymitis, occasional abortions and increased perinatal mortality (NOZAKI *et al*., 2004; SILVA et *al.*, 2009).

2 OBJECTIVE

The objective of this literature review was to address relevant aspects of brucellosis, such as some affected species, transmission routes, clinical signs, control and prevention, as well as its impacts on public and animal health.

3 METHODOLOGY

A literature review was conducted using scientific articles available in the electronic databases *PubMed*, *Science Direct*, *Scientific Electronic Library Online* - Scielo, Periódicos CAPES, Google Acadêmico, as well as books, manuals and legislation, using the descriptors: "brucellosis", "zoonosis", "animal health" and "public health", in Portuguese and English.

4 DEVELOPMENT

4.1 HUMAN BRUCELLOSIS

Human brucellosis, also known as Rippling Fever, Thousand Faces Disease or Mediterranean Fever (SANTA CATARINA, 2019), is a systemic disease that can occur in subacute, acute or chronic forms (PELERITO *et al*., 2014). Despite being considered one of the most important zoonoses worldwide by the *World Organization for Animal Health* (OIE), *World Health Organization* (WHO) and *Food and Agriculture Organization of the United Nations* (FAO), the disease remains neglected (DADAR *et al*., 2019).

Because it is a disease that is difficult to diagnose, human brucellosis is constantly underdiagnosed and, consequently, underreported (LAWINSKY *et al*., 2010). This is due to the nonspecific symptoms, which are compatible with other multisystem pathologies that affect the gastrointestinal, skeletal, nervous and cardiovascular systems (WU *et al*., 2022). As a result of misdiagnosis, treatment is often inadequate, which can prolong and aggravate the disease in the patient (ZHENG *et al*., 2018).

Among the *Brucella* species, only four affect humans. While *B. canis* tends to cause mild symptoms, the species *B. suis* and *B. abortus* are described as responsible for moderately severe conditions (QUINN *et al.*, 2007). *B. melitensis* is the most virulent

species for humans and can cause chronic infection (LAWINSKY *et al*., 2010), being considered the main cause of death due to the disease (OLSEN; BELLAIRE, 2016).

Although the lethality rate of human brucellosis (about 2%) is considered low (LAWINSKY *et al*., 2010), the prevention and control of the disease in animals is extremely important due to the risks to public health, since infection usually occurs through direct contact with infected animals or their biological materials (OLSEN; BELLAIRE, 2016), and the agent can penetrate through skin lesions, inhalation or ingestion (QUINN *et al*., 2007). Transmission to humans can occur through the consumption of contaminated food, especially *fresh* milk or its derivatives (TUON *et al*., 2017; DADAR *et al.*, 2019; SANTA CATARINA, 2019), with heat treatment being an important form of prevention due to the inactivation of the etiologic agent (DADAR *et al.*, 2019; SANTA CATARINA, 2019).

Brucellosis is considered a predominantly occupational disease (LAWINSKY *et al*., 2010), especially affecting veterinarians, slaughterhouse employees and farm workers (OLSEN; BELLAIRE, 2016) due to increased contact with secretions or excretions of infected animals (QUINN *et al.*, 2007). Veterinarians, as well as laboratory workers, can also become accidentally infected by inoculation of the pathogen with contaminated needles (LAWINSKY *et al.*, 2010; DADAR *et al.*, 2019). According to the Regional Council of Veterinary Medicine of the State of São Paulo (SÃO PAULO, 2020), it is of paramount importance to carry out adequate training by those responsible for vaccinating bovines, as well as the use of Personal and Collective Protective Equipment (PPE / PPE), since vaccines are developed with samples RB51 and B19, which are pathogenic to humans. In addition, in the event of an accident, the exposed area should be washed immediately and a health service should be sought as soon as possible.

The incubation period of brucellosis in humans can vary from 5 to 60 days (GENOVEZ, 2014) and symptoms can remain for days, months and even years if the disease is not treated properly. Infected individuals may present a clinical picture characterized by generalized malaise (LAWINSKY *et al*., 2010), fever, cough, fatigue, asthenia, adynamia, headache, weight loss, depression, sleep changes, increased sensitivity to cold, intense sweating, myalgia, tendonitis, dysuria, abdominal pain, changes in intestinal transit, skin lesions and, in acute cases, there may be involvement of various organs and tissues (GENOVEZ, 2014). About 60% of cases have osteoarticular complications, with sacroiliitis being the most common (LAWINSKY *et al*., 2010). However, many patients present asymptomatic infection (GENOVEZ, 2014).

The diagnosis of human brucellosis is mainly performed by clinical manifestations (GENOVEZ, 2014) and by the positive epidemiological history, investigating whether there was ingestion of contaminated food or contact with infected animals (SANTA CATARINA, 2019). The blood count has little diagnostic importance, and the definitive diagnosis is made through direct tests, such as blood, bone marrow, fluid or tissue culture (PESSEGUEIRO *et al*. 2003; GENOVEZ, 2014), considered the gold standard for brucellosis diagnosis (ZHENG *et al*., 2018), in addition to *Polymerase Chain Reaction (*PCR). Indirect tests for *anti-Brucella* spp. antibodies can also be used (SANTA CATARINA, 2019).

4.2 CANINE BRUCELLOSIS

In dogs and wild canids, brucellosis has a chronic character (ALMEIDA *et al*., 2004). In most cases, the etiologic agent is *B. canis*, and infection by *B. abortus is* less common (SUZUKI *et al.*, 2008).

The disease has varied clinical manifestations, with a higher occurrence of reproductive alterations, such as abortion, retained placenta, vaginal discharge, decreased fertility, embryonic death, stillbirths or birth of weak puppies. In males, epididymitis, prostatitis, testicular atrophy, scrotum dermatitis, sperm abnormalities, infertility and, sporadically, lymphadenopathy, splenomegaly, meningoencephalitis, uveitis and discospondylitis may occur (ALMEIDA *et al*., 2004), and may rarely result in lameness, paresis or paralysis (QUINN *et al.*, 2007).

Among the forms of transmission of *B. canis*, venereal transmission stands out (OLSEN; BELLAIRE, 2016). According to Suzuki *et al*. (2008), the microorganism outside the host has a short average life, but infected animals can transmit the pathogen for long periods. Females can shed *B. canis* for four to six weeks after the occurrence of abortion and the vaginal secretion of infected females can contain a number of bacteria as high as 10^{10} CFU/mL (OLSEN; BELLAIRE, 2016). Therefore, castration is considered an important form of prevention as it reduces the risk of transmission of the disease (QUINN *et al.*, 2007). Diagnosis and control of canine brucellosis is based on routine serologic tests (QUINN *et al*., 2007), with IgM antibodies indicating recent infection (MINHARRO *et al*., 2005).

4.3 BOVINE BRUCELLOSIS

B. abortus is responsible for most infections caused by the genus *Brucella* (BRASIL, 2006). Despite infecting humans, sheep, dogs and horses, *B. abortus* has a preference for the bovine species (SOLA *et al*., 2014; QUINN *et al.*, 2007). Infection in cattle occurs mainly by the digestive route (BRASIL, 2006), but other forms of contagion, such as venereal, inhalation, skin lesions or transplacental route, can also occur (QUINN *et al.*, 2007).

B. abortus has a predilection for mammary and gravid tissues and organs of the male reproductive system, due to the high production of erythritol, a hormone that attracts and stimulates the multiplication of the bacterium. The main clinical signs in males are epididymitis and orchitis, which can lead to infertility and decreased libido (BATAIER NETO *et al.*, 2009). Occasionally, the testes become softened and suppurative (BRASIL, 2006). In females, retained placenta, endometritis, mastitis and abortion may occur, usually in the final third of gestation (BATAIER NETO *et al.*, 2009). In cases of abortion, the bacterium is excreted through fetal fluids (QUINN *et al.*, 2007) and the animal remains a carrier of the disease for an undetermined period. When it affects herds, brucellosis can reduce milk production between 20 and 25% (BATAIER NETO *et al.*, 2009), in addition to reducing fertility rates (QUINN *et al.*, 2007).

The diagnosis of bovine brucellosis is usually performed by serological and bacteriological tests, since the clinical signs of brucellosis are not pathognomonic (BATAIER NETO *et al*., 2009). Confirmatory tests include: Fluorescent Polarization Test (FPA), 2-Mercaproethanol Test (2-ME) and Complement Fixation Test (CF), which can be performed in females vaccinated with the B19 sample that are 24 months of age or older, as well as in males eight months of age or older that are designated for breeding. In females vaccinated with RB51 or not vaccinated, the test must be performed on animals aged eight months or older (BRASIL, 2022).

In Brazil, the vaccination of these animals and the diagnostic methods used follow the regulations of the National Program for the Control and Eradication of Brucellosis and Animal Tuberculosis (PNCEBT), which recommends the mandatory vaccination of calves aged between three and eight months against bovine and bubaline brucellosis throughout the national territory, with the exception of the state of Santa Catarina (BRASIL, 2022).

4.4 OVINE BRUCELLOSIS

B. ovis is the main species associated with brucellosis in sheep, also known as ovine epididymitis (LIMA, 2015). The main clinical signs of the disease are fever, weakening, dyspnea (BOTELHO; ZEFERINO, 2018), reduced fertility and inflammation of the genital organs (LIMA, 2015). In females, weak or stillborn lambs, abortion or placentitis may occur, while in males epididymitis is common (BOTELHO; ZEFERINO, 2018).

The transmission of *B. ovis* can occur by transplacental route, by direct contact with infected animals, by ingestion of contaminated water and food, as well as by artificial insemination (MARTINS *et al*., 2012). Contact with excretions of infected animals can spread ovine brucellosis in the herd (LIMA, 2015), and venereal transmission is of great importance in the spread of the disease (OLSEN; BELLAIRE, 2016), and can occur between ram-sheep and ram-sheep (QUINN *et al.*, 2007). According to Botelho and Zeferino (2018), non-carrier males are infected when covering sheep previously covered by infected males, which is defined as passive venereal transmission.

B. ovis can be detected in ovine semen around 20 days after infection, with clinical signs of epididymitis detected after nine weeks (QUINN *et al.*, 2007). Females eliminate *B. ovis* by vaginal secretion and lambs born to infected mothers may develop the disease after puberty (BOTELHO; ZEFERINO, 2018). The pathogen can be identified in milk samples, genital secretions and tissues (LIMA, 2015).

Raising sheep in an intensive system increases the chances of spreading the disease, since the animals are close for long periods. In addition, *B. ovis* can persist in the environment, surviving in milk, urine and water for approximately 120 days (BOTELHO; ZEFERINO, 2018). Therefore, sanitary and hygienic measures are essential to avoid contamination and spread of the pathogen in the herd. In addition, regular examinations contribute to the detection of the disease, avoiding a significant increase in infected animals (LIMA, 2015).

5 FINAL CONSIDERATIONS

Brucellosis is a zoonosis of great impact on public and animal health, mainly due to its wide distribution and the range of susceptible individuals. Due to the habit of consuming animal products, human infection is more associated with *B. abortus*. In order to minimize the risks of animal and human infection by the pathogen, it is important that due care is taken in food intake and animal handling, especially by farmers and

veterinarians, as well as preventive vaccination whenever possible and periodic diagnostic tests on animals. In addition, examinations should be carried out when any animal shows clinical signs of the disease, preventing it from being spread throughout the herd and causing economic losses and risks to human health.

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