World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

A review on Paratuberculosis (John's disease) current diagnostic approaches and future prospects

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World Journal of Advanced Research and Reviews, 2024, 23(02), 414–416

Publication history: Received on 16 June 2024; revised on 02 August 2024; accepted on 05 August 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.23.2.2353

Abstract

The objective of the present study is to review the current diagnostic tools used for detection of paratuberculosis infection in animals. It also showed the sensitivity and specificity of each test as well as the difficulty of fecal culture as gold standard technique for paratuberculosis infection diagnosis. It also reviewed the limitation of commercial Elisa tests as they cannot be used for diagnosis of animals at early stages of infection. Lateral flow test has been recently developed. We suggest it could be used as rapid, accurate useful tool for diagnosis of MAP infection.

Keywords: Paratuberculosis; MAP; Elisa; PC; Lateral Flow (LAFs)

1. Introduction

Paratuberculosis (John's) is a chronic debilitating disease affecting ruminant livestock and is caused by *Mycobacterium avium* subsp. *paratuberculosis* (MAP). It has a huge impact on animal welfare causing both direct and indirect economic losses and arouses a serious public health concern causing Crohn's disease in humans.

MAP infects several animal species. However, the disease especially affects cattle, goat sheep, camel. In these species clinical signs consist in progressive weight loss, diarrhea, reduced milk production, infertility and eventually death.

Diagnosis of MAP infection in these animals can be made by methods based on either detection of the organism in fecal samples or detection of antibodies in serum or milk samples (Bech-Nielsen S, et, al. 1992). Fecal culture for MAP is considered the most used reference test for evaluation of serological tests because it is widely available and the most sensitive and specific test for paratuberculosis. However, it is expensive and slow, requiring 8–16 weeks for completion of testing (Collins MT, 1996). Among tests for serum antibody to MAP, enzyme-linked immunosorbent assay (ELISA) based methods are the most widely used.

Several commercial ELISA kits for bovine paratuberculosis are currently available, and multiple studies have compared their accuracy (Collins MT, Wells SJ, Petrini KR, et al: 2005, Kalis CHJ, Barkema HW, Hesselink JW, et al: 2002, McKenna SLB, Barkema HW, Keefe GP, Sockett DC: 2006, Sweeney RW, Whitlock RH, Buckley CL, Spencer PA: 1995). Limitation of these antibodies-based assay is that they cannot be used for diagnosis of animals at early stage of infection.

Currently, fecal culture is considered "the gold standard" technique for MAP infection diagnosis (Kalis, CHJ, et, al.2002). Fecal culture, although technically difficult and time consuming, will detect infected animals 6 months or more before they have developed clinical signs, which is very important since this disease has a slow progression and many animals are non-clinical carriers of disease

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While direct visualization of MAP by acid-fast staining of intestinal smears and sections is also employed, acid-fast staining has limited sensitivity and specificity as it requires a minimum of 10^6 MAP organisms per gram of tissue and non-specific staining of other acid-fast bacterial species occurs (Thoresen OF, Falk 1994). Alternatively, direct detection of MAP in infected tissue by immunohistochemistry using MAP-specific antibodies is a more accurate technique that can detect both intact and lysed MAP organisms (Coetsier C, et, al 1998).

Other diagnostic methods include polymerase chain reaction (PCR) which detects MAP in feces. The single largest problem in John's disease is the difficulty in detecting infected animals that are not showing signs of illness. PCR detecting MAP DNA in feces, have inadequate sensitivity for detecting subclinical animals.

Innovative "omics" technologies such as next-generation sequencing (NGS) technology-based RNA-sequencing (RNA-Seq), proteomics and metabolomics can be used to find host biomarkers. The discovered biomarkers (RNA, microRNAs, proteins, metabolites) can then be used to develop new and more sensitive approaches for PTB diagnosis (Seth, M, et, al 2009)

Traditional approaches for measuring host antibodies and biomarkers, such as ELISAs, northern blotting, quantitative reverse-transcriptase polymerase chain reaction (RT-qPCR), cDNA microarrays, and mass spectrometry are time-consuming, expensive, and sometimes exhibit poor sensitivity. With the rapid development of nanotechnology, low-cost monitoring devices for measuring antibodies against MAP proteins in point-of-care (POC) settings have been developed.

Lateral Flow assays (LFAs) are thought to be appropriate for on-site detection of antibodies to MAP antigens and/or host biomarkers. LFAs have recently been developed to accurately detect antibodies against MAP antigen (Manessis, G, et, al 2022).

Lateral flow assays (LFAs) are diagnostic assays based on the principles of immunochromatographic lateral flow test strips. The test sample flows along a solid substrate through capillary action, which takes 10–15 min to complete. LFAs are quick assays, which only require a few drops of a sample diluted in a buffer. LFAs are made up of a membrane (frequently made of nitrocellulose), a sample pad (made of cellulose or glass fiber), a conjugate pad (made of glass fiber), and an absorbent or wicking pad (typically a cellulose filter), all of which are laminated into a sheet of plastic known as the backing card. Future direction is the application of LFAs which could be used to monitor large numbers of animals in the field and to detect antibodies against MAP antigens (Alonso et, al. 2023).

2. Conclusion

To the best of our knowledge, this study reveiwed most of the diagnostic tools used for detection of paratuberculosis infection in animals. It also showed the difficulty of fecal culturing and the limitation of commercial Elisa used to detect antibodies of infected animals at the early stages of infection. We thought that lateral flow assay (LFAs)could be appropriate for on-site detection of antibodies to MAP antigen and/or host biomarker.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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