Preventive Veterinary Medicine 151 (2018) 57–72

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

A systematic review of current immunological tests for the diagnosis of cattle brucellosis

Marie J. Ducrotoy[a,1], Pilar M. Muñoz[b,2], Raquel Conde-Álvarez[c,2], José M. Blasco[b], Ignacio Moriyón[c,*]

[a] Division of Infection and Pathway Medicine, School of Biomedical Sciences, College of Medicine & Veterinary Medicine The University of Edinburgh, Chancellor's Building, 49 Little France Crescent, Edinburgh, EH16 4SB, UK
[b] Unidad de Tecnología en Producción y Sanidad Animal, IA2 CITA/Universidad de Zaragoza, Avenida de Montañana 930, 50059, Zaragoza, Spain
[c] Instituto de Salud Tropical (ISTUN), Instituto de Investigación Sanitaria de Navarra (IdISNA) y Depto. Microbiología y Parasitología, Universidad de Navarra, Edificio de Investigación, c/Irunlarrea 1, 31008, Pamplona, Spain

ARTICLE INFO

Keywords:
Brucellosis
Review
Diagnosis
Cattle
Vaccination

ABSTRACT

Brucellosis is a worldwide extended zoonosis with a heavy economic and public health impact. Cattle, sheep and goats are infected by smooth *Brucella abortus* and *Brucella melitensis*, and represent a common source of the human disease. Brucellosis diagnosis in these animals is largely based on detection of a specific immunoresponse. We review here the immunological tests used for the diagnosis of cattle brucellosis. First, we discuss how the diagnostic sensitivity (DSe) and specificity (DSp), balance should be adjusted for brucellosis diagnosis, and the difficulties that brucellosis tests specifically present for the estimation of DSe/DSp in frequentistic (gold standard) and Bayesian analyses. Then, we present a systematic review (PubMed, GoogleScholar and CABdirect) of works (154 out of 991; years 1960–August 2017) identified (by title and Abstract content) as DSe and DSp studies of smooth lipopolysaccharide, O-polysaccharide-core, native hapten and protein diagnostic tests. We summarize data of gold standard studies (n = 23) complying with strict inclusion and exclusion criteria with regards to test methodology and definition of the animals studied (infected and S19 or RB51 vaccinated cattle, and *Brucella*-free cattle affected or not by false positive serological reactions). We also discuss some studies (smooth lipopolysaccharide tests, protein antibody and delayed type hypersensitivity [skin] tests) that do not meet the criteria and yet fill some of the gaps in information. We review Bayesian studies (n = 5) and report that in most cases priors and assumptions on conditional dependence/independence are not coherent with the variable serological picture of the disease in different epidemiological scenarios and the bases (antigen, isotype and immunoglobulin properties involved) of brucellosis tests, practical experience and the results of gold standard studies. We conclude that very useful lipopolysaccharide (buffered plate antigen and indirect ELISA) and native hapten polysaccharide and soluble protein tests exist, provided they are applied taking into account the means available and the epidemiological contexts of this disease: i) mass vaccination; ii) elimination based on vaccination combined with test-and-slaughter; and iii) surveillance and existence of false positive serological reactions. We also conclude that the insistence in recent literature on the lack of usefulness of all smooth lipopolysaccharide or native hapten polysaccharide tests in areas where S19 vaccination is implemented is a misinterpretation that overlooks scientific and practical evidence.

1. Introduction

Bacteria of the genus *Brucella* cause brucellosis, a zoonosis of worldwide impact inducing abortions and infertility in a variety of wild life forms and domestic livestock, the latter being the most common source of human brucellosis, a grave and debilitating disease (Zinsstag et al., 2011). Cattle and small ruminants are respectively the preferential hosts of *B. abortus* and *B. melitensis*, but the latter species also infects cattle in mixed breeding systems (Corbel, 1997; Verger, 1985) and, although rarely, cattle can also be infected by some *B. suis* biovars

* Corresponding author.
E-mail addresses: marie.ducrotoy@gmail.com (M.J. Ducrotoy), pmmunnoz@cita-aragon.es (P.M. Muñoz), rconde@unav.es (R. Conde-Álvarez), jblasco@unizar.es (J.M. Blasco), imoriyon@unav.es (I. Moriyón).
[1] Present address: Ceva Santé Animale, 10 Avenue de la Ballastière, 33500-LIBOURNE, France.
[2] These authors contributed equally to this work.

https://doi.org/10.1016/j.prevetmed.2018.01.005
Received 15 February 2017; Received in revised form 22 November 2017; Accepted 16 January 2018
0167-5877/ © 2018 Elsevier B.V. All rights reserved.

Table 1
Characteristics of the main brucellosis serological tests that detect antibodies triggered by *Brucella* S-LPS.[a]

Test	Antigen[b]	Relevant epitopes	Comments
Serum agglutination in tube (SAT), SAT-mercaptoethanol and Rivanol tests.	S-*Brucella* cells	C	Quantitative tests. Because they are carried out a neutral pH, SAT does not detect the non-agglutinating fraction of IgG and IgA. Blocking antibodies can be a rare cause of prozone-like effects. Because of the misconception that vaccination induces only IgM, SAT is sometimes combined with mercaptoethanol or Rivanol to remove IgM activity.
Buffered *Brucella* antigen tests (Rose Bengal test [RBT], Card and buffered plate agglutination test [BPAT]	S-*Brucella* cells	C	A group of tests carried out at pH 3,7. Acidity converts non- agglutinating antibodies into agglutinating antibodies, so that IgM, IgG and IgA are detected and these tests are not affected by blocking antibodies (no prozone-like effect). RBT and the Card test use a *B. abortus* 19 or 1119-3 8% suspension, 30:30 µL serum:antigen mixtures and 4 min incubations at room t[a]. BPAT uses an 11% suspension of *B. abortus* 1119-3; 80: 30 µL serum:antigen mixtures and 8 min incubations at room t[a].
Complement fixation test (CFT)	S-*Brucella* cells	C	Quantitative test that detects antibodies (mostly IgG1) activating guinea pig complement.
Reverse radial (RID) or double gel (DGD) immunodiffusion	NH	C	Immunoprecipitation tests carried out at high ionic strength; not sensitive to low avidity antibodies.
Indirect ELISAs (iELISAs)	S-LPS	C and core	A group of quantitative tests that have in common the adsorption or antigen to polystyrene. This adsorption opens S-LPS aggregates exposing core and lipid A epitopes so that in practice S-LPS or S-LPS hydrolytic polysaccharides (OPS-core) yield similar results. There are differences in adsorption protocols, immunoconjugate (usually adapted to detect IgG1) and enzyme substrates.
	OPS-core	C and core	
Competitive ELISAs (cELISAs)	S-LPS	C and core	Same comments as for the iELISAs but in cELISA a monoclonal antibody competes with low avidity antibodies; at least two different monoclonal antibodies are used in different protocols/kits; cELISAs do not differentiate Ig classes.
	OPS-core	C and core	
Lateral flow immunochromatography (LFiC)	S-LPS	C and core	Adsorption to the chromatographic matrix opens S-LPS aggregates exposing core and lipid A epitopes.
Fluorescence polarization assay (FPA).	OPS-core	C and core	Fluid phase quantitative tests carried out with fluorescein labeled OPS-core; it does not differentiate Ig classes

[a] Reviewed in (Ducrotoy et al., 2016).
[b] While the bacteria recommended for whole cell suspensions are *B. abortus* strains 19 or 1119-3, NH are best extracted from *B. melitensis* biovar 1 (like strain 16 M). S-LPS (and OPS-core) can be obtained from either *B. abortus* or *B. melitensis* as they are equally suitable for cattle and small ruminant brucellosis, no matter the infecting *Brucella* species and biovar.

(Corbel, 1997; Ewalt et al., 1997; Musser et al., 2013; Szulowski et al., 2013; Tae et al., 2012). Diagnosis and vaccination are essential for control and eventual elimination and surveillance of this disease.

The diagnosis of brucellosis in cattle is based on bacteriological and immunological tests, which include DTH[3] and serological tests. In infected animals, DTH is elicited by protein antigens, and antibodies recognize the different sections of the S-LPS, mostly its O-polysaccharide or OPS, the cognate NH polysaccharide or proteins (Ducrotoy et al., 2016). Anti-S-LPS antibodies in serum include IgM, IgG and IgA. IgM dominates in the early phase but is rapidly replaced by IgG and to a lesser extent by IgA. During the early stages of infection, all these antibodies display agglutinating ability at neutral pH; as the infection evolves, non-agglutinating IgG and IgA antibodies progressively replace agglutinating antibodies. Non-agglutinating antibodies, however, become agglutinating at acid pH. Accordingly, S-LPS tests vary in their ability to detect those immunoglobulin classes, depending on pH (neutral in SAT and acid in the buffered plate agglutination tests [i.e. RBT, CT and BPAT), specificity of immuno-conjugate (immunosorbent assays) and the effect detected (agglutination, precipitation, complement consumption or primary binding; see Table 1). Vaccination, however, also elicits both DTH and antibody responses (Ducrotoy et al., 2016). The vaccines recommended by OIE are *B. abortus* S19 and *B. abortus* RB51 (OIE, 2016). Vaccine S19 elicit antibodies to the S-LPS whose intensity depends on age, dose and route of vaccination, and RB51 (a rough vaccine) triggers antibodies to the LPS lipid A-core but not to the OPS (Ducrotoy et al., 2016). Moreover, bacteria carrying OPS structurally close to the OPS of S brucellae can cause FPSR in S-LPS or OPS tests but not in protein tests (Ducrotoy et al., 2016).

There is a long list of brucellosis diagnostic tests and candidates (Ducrotoy et al., 2016; McGiven, 2013). Those that have come into use have only been the topic of partial reviews (Bale, 2002; Godfroid et al., 2010; Kaltungo et al., 2014; Nielsen, 2002; Nielsen and Yu, 2010; Poester et al., 2010; Smirnova et al., 2013) that with two exceptions (Anon., 2006; Greiner et al., 2009) have not critically examined the methodology of the studies reviewed. To fill this gap, in the present work the determination of the DSe and DSp[4] is discussed first, and then strict criteria applied to a systematic review of the literature. Similarly, no work has so far discussed the application of the tests in the different contexts of brucellosis (infection and no vaccination, mass vaccination; elimination [i.e. local eradication]) based on vaccination and test-and-slaughter, and surveillance with presence of FPSR). Thus, the systematic review is complemented by a discussion of the application of tests.

[3] Abbreviations used throughout the text: BPAT, buffered plate agglutination test; CFT, complement fixation test; CI, confidence interval; CIEP, cross-over immunoelectrophoresis; CT, card test: DGD, double gel immunodiffusion; DSe, diagnostic sensitivity; DSp, diagnostic specificity; DTH, delayed type hypersensitivity; ELISA, enzyme-linked immunosorbent assay; bELISA, blocking ELISA; cELISA, competitive ELISA; iELISA, indirect ELISA; FPA; fluorescence polarization assay; FPSR, false positive serological reactions; LFiC, lateral flow immunochromatography; LPS, lipopolysaccharide; MRT, milk ring test; NH, native hapten; OPS, O-polysaccharide; Omp, outer membrane protein; RBT, rose bengal test; RID, reverse radial immunodiffusion; ROC, receiver operator characteristic; S, smooth; SAT, standard agglutination in tube.

[4] DSe is the ratio (n° of true of positives that are positive in the test)/(total n° of true positives tested), and DSp is the ratio (n° of true of negatives that are negative in the test)/(total n° of true negatives tested). Values equal (or close) to 0.5 or 50% (if expressed as%) indicate a random (or almost random) diagnostic result. DSe is not to be confused with the analytical sensitivity that refers to the threshold level of detection of a given analyte (for example, a specific antibody) and is usually expressed in the appropriate units (for example, nanograms).

Download English Version:

https://daneshyari.com/en/article/8503509

Download Persian Version:

https://daneshyari.com/article/8503509

Daneshyari.com