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Preventive Veterinary Medicine 79 (2007) 59–69
PREVENTIVE VETERINARY MEDICINE
www.elsevier.com/locate/prevetmed

Bayesian analysis to validate a commercial ELISA to detect paratuberculosis in dairy herds of southern Chile

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Abstract

In Chile, *Mycobacterium avium* subsp. *paratuberculosis* (*Map*) has been isolated on several occasions and clinical cases have been reported. Nevertheless, diagnostic tests have not yet been validated for this agent in the Chilean setting. The objective of the study was to validate a commercial ELISA to detect Map shedding dairy cows in management conditions, prevalence and stages of infection existing in Southern Chile, utilising different statistical approaches.

Blood and faeces were collected from 1333 lactating cows in 27 dairy herds (both large commercial and smallholder dairy farms) between September 2003 and August 2004. Within the herds up to a maximum of 100 dairy cows were selected based on age ($\geq$3 years old) and, if present, clinical signs of a *Map* infection. In herds with less than 100 cows, all cows $\geq$3 years old were sampled. Blood samples were tested using a commercial ELISA kit (IDEXX Laboratories, Inc.). Faecal samples were cultured on Herrold's Egg Yolk Medium (HEYM). Latent class models (i.e. maximum likelihood (ML) methods and Bayesian inference) were used to determine the validity of the ELISA.

Map was cultured from 54 (4.1%) cows and 10 (37.0%) herds, which were all large, commercial dairy herds. As a result of empty cells in the cross-tabulations, the ML model provided the same results as the validation with faecal culture as the gold-standard. In the Bayesian model, the Se and Sp of the ELISA were estimated to be 26% (95% CI: 18–35%) and 98.5% (95% CI: 97.4–99.4%), respectively. For faecal culture, the Se was 54% (95% CI: 46–62%) and the Sp was 100% (95% CI: 99.9–100%). Interestingly, the prevalence in the smallholder dairy farms was estimated to be 8% even

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0167-5877/$ – see front matter
doi:10.1016/j.prevetmed.2006.11.005

though there were no faecal culture positive cows detected in those herds. There was no significant correlation between the two tests. The advantage of Bayesian inference is that the Se and Sp of both tests are obtained in one model relative to the (latent) true disease status, the model can handle small datasets and empty cells and the estimates can be corrected for the correlation between tests when the tests are not conditionally independent. Therefore, Bayesian analysis was the preferred method for Map that lacks a gold-standard and usually has low cow-level prevalence.

Keywords: Paratuberculosis; Test validation; Bayesian analysis; Chile

1. Introduction

The Southern regions are the main milk-producing area in Chile, producing 66% of milk for processing in Chile and with 80% of the dairy herds. Approximately, 84% of the 11,000 dairy herds in Southern Chile are considered ''smallholder'' dairy farms. These are subsistence farmers that produce <100,000 kg of milk per year (Amtmann et al., 1995). Cattle graze outside all-year round and are fed little or no concentrates. Milk is usually collected by hand and transported to a local co-operative milk collection centre where it is added to milk from other farms and cooled in a large refrigerated tank. In contrast, the medium to large commercial dairy herds in Southern Chile often have more than 200 dairy cows that are grazed all-year round but are kept inside during the nights in winter. On these medium-to-large dairy farms, progress is rapid and husbandry mimics that adopted in the USA and Europe.

Little was known about the status of herds for *Mycobacterium avium* subsp. *paratuberculosis* (*Map*) in Chile. However, clinical cases were reported and *Map* was isolated on several occasions (Kruze et al., 2000, 2001). Nevertheless, diagnostic tests were not yet validated in Chile. For successful control programs for *Map*, it is essential to have reliable diagnostics and appropriate management measures in place (Benedictus et al., 2000). The ELISA test is the most widely used test, because it is simple, rapid and cheap. Culture of faecal samples is commonly used as the reference test for *Map* because of the reported high specificity (∼100%) and reasonable sensitivity (∼50%) (Whitlock et al., 2000). Several validation studies have been carried out with the IDEXX ELISA on panels of sera with a known infection status (Dargatz et al., 2001; Collins et al., 2005). The drawback of the validation on specific panels (i.e. samples with a known infection status) is that these may not be representative of the population in which the test is going to be used (Greiner and Gardner, 2000). In a field validation, the performance of an assay should be monitored for validity in the target population and heterogeneity of the validity amongst subpopulations (Jacobson, 1998).

The sensitivity (Se) and specificity (Sp) of a test can be obtained with several statistical methods. When a perfect reference test (gold-standard) is available the Se and Sp of the test can be estimated directly. However, there is no gold-standard available for paratuberculosis. Hui and Walter (1980) developed a maximum likelihood (ML) method to estimate the Se and Sp in which two tests were simultaneously applied to individuals in two populations with different prevalences of disease. Pouillot et al. (2002) developed an online