Assessment of Methodological Quality and Source of Variation in the Magnitude of Vaccine Efficacy: A Systematic Review of Studies from 1960 to 2005 Reporting Immunization with Moraxella bovis Vaccines

M. Burns; A.M. O'Connor
VDPAM, Iowa State University, Ames, IA

Introduction

We conducted a systematic review of available literature evaluating pinkeye (Moraxella bovis) vaccines in calves to evaluate sources of variation in vaccine efficacy associated with pinkeye vaccines. The sources of variation investigated were divided into two groups: methodological study design features and study specific features.

Materials and Methods

12 electronic databases were searched in June, 2006. Other efforts to identify studies included sending a letter to pharmaceutical companies with a product labeled for pinkeye (M. bovis) immunization and hand searching The Bovine Practitioner, Proceedings of the American Association of Bovine Practitioners Annual Meeting, and World Buiatrics Congress conference proceedings since 1985. Studies considered relevant described a M. bovis vaccine used prophylactically. The outcome of interest was cases of pinkeye in individual animals (not eyes) based on clinical evaluation of eyes, not culture of M. bovis. The study population was limited to calves. Studies with no control group were excluded. Among field trials, only those conducted on beef calves were included. For descriptive purposes, a point was assigned to each trial based on the description of seven components: study population, vaccine regimen, placebo or adjuvant as the control versus non-vaccination, a case definition, frequency and duration of disease assessment, randomization or blocking when assigning animals to groups, and blinding of investigators to vaccination status. Zero indicated that none of the seven components were described. We also calculated the risk ratio for each trial. For protective vaccines, the risk ratio should be less than one. We also used meta-regression to determine if including blinding or randomization in the study report was associated with a favorable vaccine report.

Results

Data on 123 unique vaccine-to-control comparisons were extracted from 38 studies. Ignoring the use of randomization or blinding, 51 of 118 trials (43%) reported significantly protective vaccines (Risk ratio 95% CI <1). 5 studies were excluded due to non events. 15 trials reported using randomization and blinding and only 3 reported a reported significantly protective vaccines. Only 4 trials reported all 7 components of the study design and the weighted combined risk ratio was 0.55 (95% CI: 0.42-0.76, n= 4). This group of four trials came from a single group of authors and a single vaccine. Twelve trials did not report any of the seven study components evaluated and received a zero score, these studies tended to report highly effective vaccines (weighted combined risk ratio 0.32: 95% CI: 0.25-0.39, n=12)

Significance

A large number of vaccination studies failed to report fundamental features of studies that would be required to assess the quality of the study. Further, a large number of the studies failed to report features of the study execution such as dose, route, and frequency of administration that help explain why vaccines may behave differently. From our analysis, it seems that complete reporting of the study design and execution are important, as our results indicate that these qualities may be inversely related to reporting of favorable results and, therefore, the internal validity of the study outcome may be questionable.