In-vitro activity of cefitofur against Australian isolates of the family Pasteurellaceae associated with respiratory disease in cattle and pigs

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Cefitofur is a broad spectrum, b-lactamase-resistant cephalosporin (Yancey et al. 1987). Studies performed outside Australia have established that cefitofur inhibits the growth of isolates of Pasteurella multocida, Pasteurella haemolytica, Actinobacillus pleuropneumoniae, Haemophilus somnis, Escherichia coli and Salmonella rhyphimurium at concentrations of 0.25mg/ml or less (Yancey et al. 1987; Post et al. 1991; Watts et al. 1994).

A field study in Canada has demonstrated that cefitofur is effective in the treatment of natural outbreaks of respiratory disease in feedlot cattle proving superior to trimethoprim-sulphadoxine (Jim et al. 1992). In that study, cattle receiving cefitofur had a significantly lower percentage of animals requiring more than three days of treatment for the initial treatment episode compared with the cattle receiving trimethoprim-sulphadoxine.

In this paper, we report on the in vitro antibacterial activity of cefitofur against isolates of P multocida and P haemolytica (19 and 34 respectively) obtained from Australian cattle and isolates of P multocida and A pleuropneumoniae (30 and 50 respectively) from Australian pigs. The Pasteurella isolates were selected from diverse a background as possible with isolates from New South Wales (1 P haemolytica, 11 bovine P multocida and 10 porcine P multocida isolates), Queensland (33 P haemolytica, 7 bovine P multocida and 11 porcine P multocida isolates) and Victoria (1 bovine P multocida isolate and 9 porcine P multocida isolates). The isolates of A pleuropneumoniae examined were selected to represent the known genetic diversity of this species in Australia (Hampson et al 1993) and included all 7 serovars known to occur in Australia (Hampson et al 1993; Blackall and Pahoff 1995).

Representatives of the currently unserotyped isolates were also included (Blackall and Pahoff 1995). A reference strain of E coli (ATCC25922) was used as a control strain.

The minimal inhibitory concentration (MIC) of cefitofur* for the isolates was determined by a standardised agar dilution method as described previously (Stephens et al 1993) with some modifications. Firstly, the antibiotic plates did not contain lyed horse blood. Secondly, for the A pleuropneumoniae isolates, all media were supplemented with 0.0024% (w/v) reduced nicotinamide adenine dinucleotide (NADH). The agar plates contained a final concentration of cefitofur that varied from 50 mg/ml to 0.20 mg/ml. The test organisms were grown overnight in tryptose phosphate broth† plus 0.0025% NADH for A pleuropneumoniae and were diluted 10⁻³, to yield about 5 x 10⁵ colony forming units/mL (Blackall et al. 1995). One mL of this dilution was then inoculated onto the plates. A plate that did not contain any antibiotic was included with each set of organisms. All organisms were also plated onto 5% sheep blood agar to confirm the purity of the inoculum. Each plate was also inoculated with the control strain of E coli (ATCC25922). The inoculated plates were incubated aerobically at 37°C for 18 hours. The MIC was taken as the lowest concentration to prevent growth. The MIC was defined as that concentration of cefitofur that inhibited 95% of the isolates examined.

The MIC for the reference strain of E coli was always 0.78 mg/ml. This value is within the expected range (0.25 - 1.0 mg/ml) for this strain (Anon. 1990). The MICs for all the bovine and porcine P multocida, the bovine P haemolytica and the A pleuropneumoniae isolates were ≤ 0.2 mg/ml. As no isolate of any of the three species tested was capable of growing at the minimum antibiotic concentration used in this study (0.2 mg/ml), the MIC of cefitofur for all the isolates examined in this study was ≤ 0.2 mg/ml. The recommended in vitro interpretative criteria for cefitofur are as follows: growth at ≥ 8 mg/ml = resistant, growth at 4 mg/ml but no higher = intermediate sensitivity; growth at 2 mg/ml but no higher = susceptible. On the basis of these figures, all 34 isolates of P haemolytica, all 49 isolates of P multocida and all 50 isolates of A pleuropneumoniae were susceptible to cefitofur.

Similar studies, based on isolates of these species obtained from American animals, reported an MIC of cefitofur for these three species of either ≤ 0.06 mg/ml (Yancey et al. 1987; Watts et al. 1994) or ≤ 0.125 mg/ml (Post et al. 1991). The higher figure reported in our study is explained by the fact that the lowest antibiotic dilution used in our study was 0.2 mg/ml. In both our study and the three previous studies (Yancey et al. 1987; Post et al. 1991; Watts et al. 1994), all isolates examined have been found to be susceptible to cefitofur. The results of our study have provided evidence that cefitofur is highly effective in vitro against Australian bovine and porcine isolates of Pasteurella spp and porcine isolates of A pleuropneumoniae.

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References
Anon (1990) National Committee for Clinical Laboratory Standards Document M7-A2, Villanova, USA

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* Cefitofur sodium, Lot No. 555-1212, Upjohn Company, Kalamazoo, USA
† Oxoil CM283, Oxoid Australia Pty Ltd, West Heidelberg, Vic

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