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Concentrations of methicillin in blood, normal milk and mastitic milk of cows after intramuscular injection of methicillin and tamethicillin

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Tamethicillin (TAM) is a basic ester pro-drug of methicillin (MET) which is converted in the body by non-specific esterases to MET. Equal doses of MET and TAM were administered intramuscularly in a crossover trial involving four dairy cows. Acute mastitis was induced in each cow by infusing two quarters of the udder with *Escherichia coli* endotoxin 3 h before antibiotic administration.

Peak serum MET concentrations after MET injection were significantly ($P<0.001$) higher than peak serum drug concentrations after TAM injection. The $t_{1/2}$ of MET in serum after MET and TAM treatments were 18 min and 2 h, respectively. Normal milk MET concentrations during the first 8 h after TAM administration were significantly ($P<0.05$) higher than after MET treatment. Mastitic milk MET concentrations during the period 2–6 h after MET injection were significantly ($P<0.01$) higher than after TAM administration. However, MET concentrations which were equal to or higher than the minimal inhibitory

infusion. Infusion of saline did not result in any inflammatory reaction in the infused quarters. After intracisternal administration of vehicles, some changes in inflammation parameters were evident in all groups.

Somatic cell count showed a slight increase in most of the quarters treated with oils. Table I gives the mean SCC in all treated and respective control quarters in relation to the time of infusion. Soybean oil caused a rise in all four infused quarters which peaked 2–3 days post-infusion and was still present during the final examination 1 week later. The response caused by other vehicles was milder, except in the quarter which became infected. Excluding this case, the number of somatic cells in individual quarters generally did not increase more than 10-fold.

Mean NAGase values before and after infusion are given in Table II. Only sporadic changes in milk NAGase were noted and they

The problem of the indirect markers is the individual variation caused by such effects as inter-animal variation, lactation stage, lactation number and environmental factors. These tend to mask any effects due to provoked tissue irritation. This problem can be partly overcome by comparing the test quarter with other quarters of the same cow (Sheldrake *et al.*, 1983; Mattila & Sandholm, 1985). However, local therapy may cause a response in the control quarters as well. This would decrease any difference between the treated and control quarters. Another evaluation method would be to use pretreatment values of the infused quarters as reference values, so that differences between the basal levels of two quarters in a cow would be eliminated (Rehm, 1983; Fox *et al.*, 1986).

In this study the post-infusion values were compared with the pre-treatment values of the same quarters as well as values of the

tration of commercial mastitis remedies. Kitchen, B.J., Middleton, C. & Salmon, M. (1978)