BENEFICIAL EFFECTS OF ENDOTOXIN INDUCED TOLERANCE IN EXPERIMENTAL E. COLI MASTITIS

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E. coli MASTITIS in cattle can result in a dysregulated, overshooting immune response causing high economic losses worldwide. Lipopolysaccharide (LPS) is regarded as the main pathogen associated molecular pattern (PAMP) of E. coli. It is recognized by toll like receptor (TLR) -4, followed by the production of proinflammatory signals. If a host is repeatedly confronted with PAMPs the immune response might be markedly decreased. This mechanism is known as endotoxin tolerance (ET). In this study, based on a well defined MASTITIS model, midlactating heifers were initially treated by intramammary administration of 1µg LPS (“priming”) in all quarters. 72 hours (n=5) or 10 days (n=10) later, animals were challenged with 500 CFU E. coli into the quarter with the lowest somatic cell count (SCC). Animals of the control group (n=5) were challenged without “priming”. All control animals showed acute clinical MASTITIS with fever (41.1±0.5°C), udder swelling and altered milk secretion (clots) within 15h. In contrast, animals “primed” 72h before challenge showed normal general health condition and normal temperature (< 39.2°C) and no signs of clinical MASTITIS. The animals infected with E. coli 10d after “priming” showed milder clinical symptoms compared to the control group, but more severe than in the 72h “primed” group. In mammary tissue of control animals the factors TNFα, CXCL8, CCL20, LAP, SAA and IRAK-M were significantly increased 24h after E. coli challenge (P< 0.009), as assessed by qRT-PCR. In comparison, animals “primed” 72h before challenge showed significantly lower levels for CXCL8, SAA and IRAK-M whereas those “primed” 10d before challenge only showed a reduction for IRAK-M. In non challenged udder quarters sustained elevated levels of Lingual antimicrobial peptide (LAP) were still present 10d after priming, explaining the limited inflammatory response and enhanced bacterial clearance in primed animals. These results show for the first time, that an induced tolerance towards LPS may beneficially modulate inflammation and plays a protective role in bovine MASTITIS. (Supported by PFIZER Animal Health Europe)

Keywords: MASTITIS, LPS, tolerance, TLR, E. coli