

Concentrations of azithromycin in target tissues relevant for non-tuberculous mycobacteria treatment: *an experimental porcine model*

Background

Azithromycin is a widely used antibiotic and typically the backbone drug in co-administration with multiple other antibiotics in the treatment of complicated infections with non-tuberculous mycobacteria (NTM). NTM a group of opportunistic bacteria, comprised of more than 190 species and subspecies, that cause serious pulmonary and extrapulmonary infections. NTM are very resilient, and even when administering multiple antibiotics over a period of 12-18 months relapses are common. In recent years the incidence of NTM-infections has been on the rise, and with a 40% 5-year mortality when infected, these infections are a global health challenge.

The concentration of azithromycin has never been directly measured in tissues relevant for NTM-infection. It is of great concern to ensure that therapeutic levels are reached in the treatment of NTM when these are treated for so long. Microdialysis is the method of choice for mapping real-time tissue concentrations. Specifically, microdialysis is very advantageous by providing dynamic sampling of unbound antibiotics simultaneously from multiple target tissues.

Methods

Sixteen pigs will be randomised into two groups of eight and receive different treatment regimes. Group one will receive azithromycin in monotherapy. Group two will receive azithromycin as group one and in addition to this rifampicin and ethambutol. Samples from the lung, muscle, subcutis, tendon sheath, cortical bone and knee joint will be collected using microdialysis. Microdialysis is a probe-based method that allows for continuous sampling of unbound water-soluble molecules across a semipermeable membrane at the tip of the probe. The concentration of azithromycin will be determined hereafter. Based on this analysis the AUC/MIC ratio will be determined for relevant NTM, the concentration of azithromycin is at therapeutic level if AUC/MIC-ratio >10.

Results/conclusion

The study has not yet been performed