UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

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1) Project title

Role of PharmacoDynamic/PharmacoKinetic Factors in Antibiotic Response to Male Accessory Gland Infections

2)Abstract (max 500 words)

Male accessory gland infection (MAGI) is a common andrological disease, characterized by symptoms of inflammation of the prostate, seminal vesicles, vas deferens and epididymis. Among the etiological agents responsible for MAGI, atypical bacteria such as Ureaplasma Urealyticum, Chlamydia Trachomatis and Mycoplasma Hominis are those most frequently identified by microbiological tests.

Importantly, MAGI are frequently asymptomatic and associate with up to 15% of male fertility disorders. Mechanistically, it is shared hypothesis that the inflammatory microenvironment that accompaining the infection associated with altered secretory activity of the accessory glands, anatomical obstructions of the ejaculatory ducts and oxidative stress on spermatozoa, ultimately leading to reduced fertility potential.

The treatment of MAGI involves the use of antibiotics only, as recommended by the European Urology Guidelines. Fluoroquinolones are considered the first choice drugs because of their wide activity spectrum, towards both typical and atypical pathogens, and for favorable pharmacokinetic properties. Tetracyclines are also used for sensitivity of atypical bacteria. However, antibiotic treatment is not able to eradicate the infection in a variable proportion of up to 40%-50% of patients, resulting in a persistent infection, that is detected in semen culture after treatment, and prone to develop antimicrobial resistance (AMR). No progostic parameter positive outcome in MAGI antimicrobial treatment has been identified yet.

The reference parameter for the evaluation of the systemic exposure to a drug is its plasma concentration. However, anatomical, inflammatory or traumatological factors may hamper the specific tissue penetration of a therapeutic agent. In particular for antibiotics, the efficacy of the therapy is strictly linked to the achievement of tissue concentrations of the drug greater than or equal to the minimum inhibitory concentration (MIC) for a given microorganism. if this condition is not reached, in addition to therapeutic failure, there is an increased risk of development of antibiotic resistance, with serious consequences regarding the indication of a given therapeutic agent for the infectious pathology. To date, there are no available studies relating the outcome of antibiotic therapy in MAGI with the levels of systemic and local exposure to the antibacterials commonly used for this clinical condition.

The adequacy of antibiotic therapy can be rationalized by monitoring a series of clinically useful pharmacodynamic (PD) parameters, such as MIC, and pharmacokinetic parameters (PK), such as drug concentrations in plasma/biofluid at representative time-poins after dosing The primary objective of the study is to evaluate the possible association between the failure of amntimicrobic treatment MAGI and the inadequate tissue exposure to the antibiotic agent of choice to eradicate the pathogen. The inadequate male accessory gland exposure to the antibiotic agent will be assessed through the quantification of PD/PK parameters, and correlated with the treatment outcome of MAGI. This would represent a novel and unprecedented approach to address a major clinical demand and to reduce the risk of AMR development.