TITLE: ANALYSIS OF THE INVOLVEMENT OF VIRULENCE GENES AND THE INFLUENCE OF SUBINHIBITORY CONCENTRATIONS OF ANTIMICROBIALS IN STRAINS OF *Staphylococcus Saprophyticus*

AUTHORS: PAIVA-SANTOS, W.; VASCONCELOS, A. B.; GIAMBIAGI-DEMARVAL, M.

INSTITUTION: Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ (Avenida Carlos Chagas Filho, 373 - Cidade Universitária. Rio de Janeiro – RJ. CEP: 21941-902.) - Brasil

ABSTRACT:

Staphylococcus saprophyticus is an important pathogen responsible for community urinary tract infections. Although some virulence determinants have been studied, such as D-serine deaminase, urease and cell-wall associated proteins, the true role of some virulence-associated genes and its distribution among *S. saprophyticus* strains are still poorly understood. It should be noted that the recurrent urinary tract infections (rUTI) are generally treated with the long-term of low doses of antimicrobials which can modulate gene expression, modify bacterial phenotypes and cause an increase in virulence. Therefore, the present study aims to evaluate the influence of subinhibitory concentrations of antimicrobials in clinical strains of *S. saprophyticus*, the involvement of virulence genes in the internalization of *S. saproph*yticus by host cells and investigate the pathogenic potential of strains isolated from different sources. The influence of antimicrobial subinhibitory concentrations was evaluated examining the expression of virulence-associated genes by real time quantitative PCR. The minimum inhibitory concentrations (MIC) for ciprofloxacin were determined, by broth microdilution method, for the clinical strain *S. saprophyticus* 7108. It was considered sensitive to the antimicrobial (breakpoint ≤1), showing MIC = 0.5 µg/ml. The expression of the *ssp* and *sdrI* genes increased in response to ciprofloxacin while the expression of *uafA* gene was downmodulated. To analyze the pathogenic potential of strains of *S. saprophyticus,* the presence of virulence-associated genes in clinical (n = 76), colonizing (n = 23), environmental (n = 30) and foodborne strains (n = 13) was investigated by PCR. In every tested strain, the presence of genes encoding the surface proteins UafA, Aas, Ssp and SssF and the DsdA and UreC enzymes was detected. In contrast, the gene encoding SdrI surface protein was not found in any of the strains. The analysis of the participation of *ssp* and *sdrI* genes in the virulence of *S. saprophyticus* is in progress and will be performed through the interaction of wild type and mutant strains with the human bladder carcinoma cell line 5637. The obtained results will provide information about the effectiveness of treatment with low doses of antimicrobials and the participation of some virulence genes during infection by *S. saprophyticus*. Furthermore, the analysis of strains from different origins may reveal a possible signature of uropathogenic strains.

Keywords: *Staphylococcus saprophyticus*, virulence genes, subinhibitory concentrations, ciprofloxacin, uropathogenic potential.

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