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Infected foot ulcers in male and female diabetic patients: a clinico-bioinformative study.

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Abstract

BACKGROUND:

The study aimed at (i) characterizing the mode of transmission of bla(CTX-M) and bla(TEM-1) among extended-spectrum-beta-lactamase (ESBL)-producing Escherichia coli strains isolated from infected diabetic foot ulcers, and (ii) identifying the risk factors for "sex-associated multidrug resistant Gram-negative bacterial (MDRGNB)-infection status" of the ulcers.

METHODS:

Seventy-seven diabetic patients having clinically infected foot ulcers were studied in a consecutive series. The E. coli strains isolated from the ulcers were screened for bla(CTX-M), bla(TEM-1), armA, rmtA and rmtB during the 2-year study-period. PCR amplified bla(CTX-M) genes were cloned and sequenced. Enterobacterial repetitive intergenic consensus (ERIC)-PCR was used for the analysis of genetic relatedness of the ESBL-producers. Risk factors for "sex-associated MDRGNB-infection status" of ulcers were assessed. Modeling was performed using Swiss-Model-Server and verified by Procheck and verify3D programmes. Discovery Studio2.0 (Accelrys) was used to prepare Ramachandran plots. Z-scores were calculated using 'WHAT IF'-package. Docking of cefotaxime with modeled CTX-M-15 enzyme was performed using Hex5.1.

RESULTS:

Among 51 E. coli isolates, 14 (27.5%) ESBL-producers were identified. Only 7 Class1 integrons, 2 bla(CTX-M-15), and 1 bla(TEM-1) were detected. Ceftazidime and cefotaxime resistance markers were present on the plasmidic DNA of both the bla(CTX-M-15) positive strains and were transmissible through conjugation. The residues Asn132, Glu166, Pro167, Val172, Lys234 and Thr235 of CTX-M-15 were found to make important contacts with cefotaxime in the docked-complex. Multivariate analysis proved 'Glycemic control at discharge' as the single independent risk factor.

CONCLUSIONS:

Male diabetic patients with MDRGNB-infected foot ulcers have poor glycemic control and hence they might have higher mortality rates compared to their female counterparts. Plasmid-mediated conjugal transfer, albeit at a low frequency might be the possible mechanism of transfer of bla(CTX-M-15) resistance marker in the present setting. Since the docking results proved that the amino acid residues Asn132, Glu166, Pro167, Val172, Lys234 and Thr235 of CTX-M-15 (enzyme) make important contacts with cefotaxime (drug) in the 'enzyme-drug complex', researchers are expected to duly utilize this information for designing more potent and versatile CTX-M-inhibitors.

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