Analisis mutasi gen Dihiydrofolate Reductase (dfr) dan Dihydropteroate Synthase (sul) pada Escherichia coli dari infeksi saluran kemih dengan fenotip Resisten Trimetoprim-Sulfametoksazol = Mutation analysis of the dihydrofolate reductase (dfr) and dihydropteroate synthase (sul) genes in E. coli isolated from the urinary tract with a trimethoprim-sulfamethoxazole resistant phenotype

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Abstrak

Trimetoprim-sulfametoksazol (TMP/SMX) merupakan golongan antibiotik lini pertama yang digunakan untuk pengobatan infeksi saluran kemih. Antibiotik TMP/SMX bekerja dengan menghambat reaksi enzimatik sintesis folat bakteri pada dua tahap yang berurutan pada bakteri, sehingga kombinasi obat ini dapat memberikan efek sinergi. Gen dfr dan gen sul merupakan gen yang mengkode DHFR dan DHPS yang terdapat di Mobile Genetic Element (MGE) yang keberadaannya dapat meningkatkan kejadian resistensi bakteri terhadap antibiotik trimetoprim-sulfametoksazol. 8 isolat Escherichia coli diketahui resitensi terhadap trimetoprim-sulfametoksazol secara fenotipik diperiksa keberadaan MGE dfr1, dfr5, dfr7&17, sul1 dan sul2 melalui metode PCR konvensional, dilanjutkan dengan analisis asam amino untuk melihat ada atau tidaknya mutasi. 7 dari 8 isolat Escherichia coli yang reistensi antibiotik trimetoprim-sulfametoksazol memiliki MGE dfr dan sul yang berkesesuaian dengan fenotipik resistensi trimetoprim- sulfametoksazol. Mutasi asam amino dijumpai pada gen dfr1 isolat no 95 pada posisi I55V; D64S; N65D; I70V; N129S. dfr5 Isolat nomor 14, 53, 88 dan 95 memiliki jumlah mutasi asam amino sebanyak 10 titik pada posisi: A17G; A20S; D21N; N22D; I26V; P29Q; Y36D; Y37D; L41F; D43G. sedangkan gen sul2 isolat 14, 29, 78, 79 dan 88 mutasi pada posisi G8W dan I12M. Keberadaan MGE dfr dan sul pada isolat klinis menunjukkan adanya mekanisme resistensi ekstrinsik bakteri yang memerlukan perhatian khusus terhadap peningkatan kejadian resistensi bakteri.

.....Trimethoprim-sulfamethoxazole (TMP/SMX) is a class of first-line antibiotics used for the treatment of urinary tract infections. TMP/SMX antibiotics work by inhibiting the enzymatic reaction of bacterial folate synthesis at two successive stages in bacteria, so that this drug combination can provide a synergistic effect. The dfr gene and sul gene are genes that code for DHFR and DHPS found in the Mobile Genetic Element (MGE) whose presence can increase the incidence of bacterial resistance to the antibiotic trimethoprim-sulfamethoxazole. 8 isolates of Escherichia coli known to be resistant to trimethoprim-sulfamethoxazole phenotypically examined for the presence of MGE dfr1, dfr5, dfr7&17, sul1 and sul2 through conventional PCR methods, followed by amino acid analysis to see the presence or absence of mutations. 7 of the 8 isolates of Escherichia coli that were trimetoprim-sulfamethoxazole antibiotic retention had MGE dfr and sul corresponding to the phenotypic resistance of trimethoprim-sulfamethoxazole. Amino acid mutations were found in the dfr1 gene isolate no 95 at position I55V; D64S; N65D; I70V; N129S. dfr5 Isolates number 14, 53, 88 and 95 have a number of amino acid mutations of 10 points at position: A17G; A20S; D21N; N22D; I26V; P29Q; Y36D; Y37D; L41F; D43G. while the sul2 gene isolates 14, 29, 78, 79 and 88 mutations at the G8W and I12M positions. The presence of MGE dfr and sul in clinical isolates suggests the existence of a mechanism of bacterial extrinsic resistance that requires special attention to the increased

incidence of bacterial resistance.