Penetration of cotrimoxazole components into skin after a single oral dose. Theoretical versus experimental approach.

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Concentrations of trimethoprim and sulfamethoxazole in plasma, cantharidin-induced skin blister fluid and theoretical peripheral compartment were determined in twelve male subjects suffering from bacterial skin diseases after a single oral dose of 0.32 g of trimethoprim and 1.6 g of sulfamethoxazole. Maximum trimethoprim concentrations of 8.5 ± 1.1 μmol/l in plasma, 5.6 ± 0.8 μmol/l in blister fluid and 5.8 ± 2.2 μmol/l in theoretical peripheral compartment were found after 3 ± 1, 7 ± 2 and 9 ± 6 h, respectively. Degree of penetration into blister fluid and theoretical peripheral compartment was 0.94 ± 0.23 and 1.05 ± 0.09, respectively. The differences between respective pharmacokinetic parameters of trimethoprim in blister fluid and theoretical peripheral compartment were statistically insignificant. Maximum sulfamethoxazole concentrations of 295 ± 47 μmol/l in plasma, 182 ± 46 μmol/l in blister fluid and 239 ± 58 μmol/l in theoretical peripheral compartment were found after 3 ± 1, 8 ± 2 and 7 ± 4 h, respectively. Degree of penetration into blister fluid and theoretical peripheral compartment was 0.82 ± 0.20 and 1.04 ± 0.02, respectively. In contrast to trimethoprim, the differences between respective pharmacokinetic parameters of sulfamethoxazole in blister fluid and theoretical peripheral compartment, except time to maximum concentration, were statistically significant. Cantharidin-induced skin blister fluid method can be used to estimate drug penetration into skin. Due to differences between the respective pharmacokinetic parameters in experimental and theoretical peripheral compartment, in some cases evaluation of drug penetration into skin should not be replaced by the theoretical peripheral compartment calculation.

Key words: trimethoprim, sulfamethoxazole, plasma concentration, skin blister fluid concentration

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