S20-04

DOSE-RELATED REFERENCE RANGES FOR THERAPEUTIC DRUG MONITORING IN HUMAN BLOOD SPECIMENS

E. Haen, C. Greiner

Clinical Pharmacology, Dept. of Psychiatry, Psychosomatic and Psychotherapy, University of Regensburg, Regensburg, Germany

A dose related reference range is calculated as a concentration range within that a drug concentration has to be expected in human blood specimens under medication with a given dose of the drug. The calculation is based on the direct correlation of the drug dose De (constant dose under long term therapy) to its blood concentration c with the total clearance of the drug (Clt) being the correlation coefficient (De = D / t = c x Clt). The clearance is taken as arithmetic mean ± standard deviation from phase II clinical trials of the drug. Thus the dose related reference range will statistically contain 68,27 % of all the drug concentrations determined under normal condition in the blood of a normal patient, where “normal” is defined as the patient population in the respective phase II clinical trial. It usually consists of patients 18-65 years of age without relevant comorbidity, comedication, and genetic abnormalities in drug metabolism. Therefore, any drug concentration determined outside its dose-related reference range creates a signal to alert for individual abnormalities in a patient such as drug-drug-interactions, gene polymorphisms that give rise to slow/rapid metabolizers, altered function of the excretion organs liver and kidneys by age and/or disease, compliance problems, a missing pharmacokinetic steady state and even signal overlay in the laboratory analysis. A table listing factors that allows the calculation of dose-related reference ranges for all relevant psychopharmaca will be included in the first update of the TDM consensus guideline to be published in Pharmacopsychiatry.

https://doi.org/10.1016/S0924-9338(09)70342-6 Published online by Cambridge University Press