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Population pharmacokinetics of Baclofen in alcohol-dependent patients

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Abstract

Baclofen is a GABA-B receptor agonist used in the treatment of spasticity. Baclofen is currently used off-label to decrease craving of alcoholic patients. However, its optimal use in these patients requires further pharmacokinetic information. The objective of this study was then to characterize the pharmacokinetics of baclofen in alcohol dependent patients.

Thirty seven outpatients (weight: 74.0 kg [42.0 - 104.0]; Age: 49 years [31 – 68]) followed in the addiction department were studied. Total mean dose of 77.9 mg (30 - 240) per day was administered by oral route. Therapeutic drug monitoring allowed the measurement of 139 plasma concentrations. The following covariates were evaluated: demographic data (age, body weight, height, sex), biological data (creatinine, urea, AST, ALT, albumin, PR, VGM, PAL, CDT, GGT) and tobacco consumption (number of cigarettes and Fagerstrom test). A non-linear mixed effects modeling (NONMEM 7.2 software) was used for the pharmacokinetic analysis.

Data were modelled with a one-compartment pharmacokinetic model. The population typical mean (percent relative standard error (%RSE)) values for clearance (CL), volume of distribution (V) and constant of absorption (Ka) were 10.3 L/h (6.3%), 81.1 L (12.1%) and 3.61 h-1 (50.4%), respectively. The between patient variability of CL (%RSE) and V (%RSE), and the residual variability (%RSE) were 53.9% (24.7%), 73.5% (45.5%) and 0.1 mg/l (20.0%), respectively.

The pharmacokinetic parameters of baclofen were estimated in patients with alcohol dependence. The kinetic was linear from 30 to 240 mg per day. However a wide between patient variability of baclofen pharmacokinetic parameters was found which was not explained by the covariates. This variability of drug exposure after baclofen administration may lead to variability among patients in drug response.

Biography

Dr. Nicolas Simon is associate director of the addiction department of Sainte Marguerite Hospital and is the Professor of the clinical pharmacology department in the medical school of Marseilles, France. He completed a M.D. Degree in Medicine in 1993 and a PhD from University of Paris in 1997. After his studies he was a postdoctoral fellow in the GlaxoWellcome clinical pharmacology unit in London for one year (1998). He was then appointed as Professor in Aix-Marseille University. Up to 2008 he was an expert of the French Drug Agency (afssaps). In 2011 he was received as adjunct Professor in the Mount Sinai School of Medical, New York. He is a member of the French Society of Pharmacology and Therapeutics and of the French Society of Alcohology. He is serving as an editorial board member of "Therapeutic Drug Monitoring", has been a reviewer for several reputed journals, and has authored 2 books and over 70 original research publications.

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