Pharmacokinetic-Pharmacodynamic Modeling of Risperidone Effects on Electroencephalography in Healthy Volunteers

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The authors investigated the changes of quantitative EEG findings with the administration of risperidone, a benzisoxazole antipsychotic drug, to elucidate the model explaining the relationship between the plasma risperidone concentration and the risperidone effect on EEG. The subjects were 9 healthy male volunteers who were without any drugs for more than 2 weeks prior to the study, and had no psychiatric diseases and other medical or neurological diseases. Blood samplings and QEEG recordings were done at baseline and 10 times after single oral administration of 1mg risperidone or placebo(15min, 30min, 1h, 2h, 3h, 4h, 6h, 8h, 12h, 24h) in a single-blind placebo-controlled design. Plasma levels of risperidone and its active metabolite 9-OH-risperidone were measured by radioimmunoassay. Selecting artifact-free portions of the EEGs from the recording with 21 electrodes according to 10−20 system, we analyzed 3 QEEG parameters : absolute power, interhemispheric asymmetry and interhemispheric coherence of 4 frequency bands(delta, theta, alpha and beta).

Our results showed that absolute powers of delta and theta frequency bands were higher in all EEG leads after the risperidone administration compared to placebo, and the maximum effect was detected at about 3 hours after drug intake in each subject. But, there were no significant differences in absolute powers of alpha and beta frequency bands as well as in interhemispheric asymmetries and coherences of all frequency bands, compared with placebo. Since there were time lags of 0.27−1.28 hour between the plasma risperidone concentration and the drug effect on EEG, which is the difference in absolute powers of delta and theta frequency bands between risperidone and placebo, the hysteresis was shown in the plasma concentration-effect curve. Postulating a first-order process of the drug movement between the plasma and effect compartments, the relationship of the effect compartment concentration with the risperidone effect on EEG was explained well by the linear model.