Oral

[O25-2] O25-2: CNS and miscellaneous

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[O25-2-1] CYP2C19 polymorphism affects the efficacy but not drowsiness in the low dose clobazam therapy

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Background

We have reported that the serum concentration of clobazam (CLB) active metabolites (N-desmethylclobazam: N-CLB) increases in *CYP2C19* poor metabolizers (PMs) and some of them need only less than 10 mg dose. The incidence of *CYP2C19* PMs is higher in Asian (about 20%) than in Caucasian or blacks. In this study, we analyzed the relationships between the degree of drowsiness and N-CLB concentrations or *CYP2C19* polymorphism in epileptic patients with low-dose CLB therapy.

Method:

Study subjects were 39 epileptic patients treated with CLB in Kyoto University Hospital. They were assessed for drowsiness using Epworth Sleepiness Scale (ESS) and divided into two groups; patients with 10 points or less (n=30) and patients with more than 10 points (n=9). Their clinical data including age, dose of CLB, serum concentrations of CLB and N-CLB, concomitantly used anti-epileptic drugs (AEDs), and genetic information for *CYP2C19* and *CYP3A5* were retrospectively obtained.

Results

Median clobazam dose was not significantly different between two ESS score groups (<10 *versus* >11: 5 (1.25-20) *versus* 7.5 (1.25-15) mg/day). Both serum concentrations of CLB and N-CLB were also not significantly different between two groups. Although *CYP2C19* genotype frequency did not show a statistical significance between two groups (*P*=0.085), all *CYP2C19* PMs (n=8) were included in the group with ESS score of 10 points or less. *CYP2C19* PMs showed a significantly higher serum N-CLB concentration, inducing a significantly higher seizure-reduction rate compared with *CYP2C19* EMs and IMs, but which was not reflected in drowsiness.

Conclusion

CYP2C19 PMs treated by low-dose of CLB acquired a higher clinical effect and comparable drowsiness compared with *CYP2C19* EMs and IMs. Pharmacological potency of N-CLB to CLB might be different between anticonvulsant effects and drowsiness, and a new strategy to specifically increase the N-CLB concentration is suggested in the combination therapy of AEDs.