

## Autoinduction of Carbamazepine Metabolism in Korean

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To evaluate the autoinduction of carbamazepine(CBZ) metabolism in Korean, pharmacokinetics of CBZ was studied in 12 Korean healthy male volunteers. There were two phases of drug administration with a wash-out interval of two weeks, 400mg CBZ was taken orally in a single dose phase, and 200mg once a day was given for 2 weeks in multiple dose phase. Blood samples were drawn serially upto 96 hours after the last dose of CBZ in each phase, and CBZ and it's metabolites, CBZ-10, 11-epoxide(CBZE) and CBZ-10, 11-diol(CBZ-diol) concentrations were determined by HPLC. Pharmacokinetic parameters were estimated using compartmental and noncompartmental analysis.

Ten days after multiple CBZ dose, there were no more significant changes of trough CBZ level in most subjects. In the multiple dose phase, oral clearance( $Cl/F$ ;  $35.08 \pm 5.32$ ) was significantly increased compared to that of single dose phases( $21.14 \pm 4.16$ ). Despite of no significant change of volume of distribution( $Vd/F$ ), the mean CBZ half-life was also significantly shortened after multiple dose(single vs multiple;  $48.29 \pm 7.32$  vs  $26.97 \pm 4.87$ ). The total AUC ratios of CBZE/CBZ were  $0.09 \pm 0.05$  at single-dose,  $0.15 \pm 0.04$  at multiple dose and of CBZ-diol/CBZ were  $0.07 \pm 0.06$  at single dose( $p < 0.01$ ),  $0.13 \pm 0.03$  at multiple dose studies( $p < 0.01$ ), and renal clearance of CBZ-diol( $Cl_R$ (CBZ-diol)) was not changed significantly.

These results seems to give a first data to evaluate the time course and the extent of CBZ autoinduction in Korean.