



Time-Dependent and Concentration-Dependent Upregulation of Carbamazepine Efflux Transporter. A Preliminary Assessment from Salivary Drug Monitoring

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SUMMARY. The aim of the present study was to detect efflux transporter induction at salivary glands. Six healthy volunteers were involved. On the first day subjects received a single carbamazepine (CBZ) dose of 400 mg. Couples of salivary samples (first and second fraction, S1 and S2) were collected throughout time after dosing. The following 6 days subjects received 200 mg every twelve hours, and morning pre-dose samples were collected. After dosing on day 7 a similar sampling schedule was carried out. CBZ and its main metabolite (carbamazepine-10,11-epoxide: EPOX) salivary levels were determined by HPLC. CBZ half-life and areas under concentration-time curves (AUC) decreased from 36.9 h to 25.7 h, and from 77.8 mg.h/L (AUC_{0-inf}) to 42.9 mg.h/L (2xAUC₀₋₁₂) between days 1 and 7. S2 and S1/S2 concentration ratio showed the same profiles all along the study period, presenting in average a 48-hours delay interval between their respective maximum values. This behavior revealed a time-dependent and concentration-dependent inductive effect of CBZ.

KEY WORDS: Carbamazepine, Efflux transporter induction, Saliva drug levels.

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