25 - E. Typical antipsychotics

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© SPMM Course to about 75mL/min. The active CBZ-10,11-epoxide (CBZ-E) metabolite has a half-life of about 6 hr. The conventional form needs to be given in multiple divided doses while extended release can be given twice a day. A steady-state plasma concentration of 4 to 12 ng/ml is therapeutic. Verapamil and diltiazem can increase carbamazepine levels and cause clinical toxicity, but this does not occur with other calcium channel blockers nifedipine and nimodipine. Also, carbamazepine decreases nimodipine and felodipine levels. Valproate inhibits epoxide hydrolase, increasing the plasma carbamazepine-epoxide levels, often without altering total plasma carbamazepine levels. Valproate also displaces carbamazepine from plasma proteins, increasing free carbamazepine. Patients can have neurotoxicity due to elevated plasma carbamazepine - epoxide levels in spite of normal plasma total carbamazepine levels. Carbamazepine reduces warfarin efficacy. Erythromycin can produce carbamazepine toxicity. Gabapentin has no significant mood stabilizing effects though it is useful to treat anxiety in bipolar patients. It is not bound to plasma proteins, is not metabolized and is 100% excreted in the urine. Gabapentin has a half-life of about 6 hrs (4 to 9) and a clearance similar to that of creatinine (120 ml/min, similar to the glomerular filtration rate), so that increased physical activity may increase GBP clearance. The bioavailability of gabapentin is not dose-proportional; it decreases as the dose increases. When gabapentin is given in 3 divided doses, at 900 mg per day the bioavailability is approximately 60%, but at 2400 mg per day it drops to 34% and at 4800 mg per day it is only 27%. Gabapentin does not induce or inhibit hepatic metabolism. It is not bound to plasma proteins and displays linear pharmacokinetics at usual dosages. Consequently, drugdrug interactions are not an issue with gabapentin. It is usually given three times a day. In patients with normal renal function, steady state is reached after 1 to 2 days of taking a stable dose of gabapentin. The dose that a patient takes should not be increased until steady state has been reached (or some time later) so that the effects of the previous dosage can be assessed.

Lamotrigine achieves peak concentrations within about 3 hours postdose with an oral bioavailability of about 98%. It is 56% plasma protein bound with t½ of 24 to 36 hours. Enzymeinducing drugs (phenytoin, phenobarbital or carbamazepine) reduce the half-life of lamotrigine whereas valproate increases the half-life. Lamotrigine itself does not affect CYP450 in most cases but increases levels of carbamazepine-10,11-epoxide, the metabolite of carbamazepine. E. Typical antipsychotics: Typical antipsychotics are well absorbed when administered both orally or parenterally. Peak plasma levels are reached in 30 min after intramuscular injection and 1 to 4 h after oral injection. Steady state is achieved in 3 to 5 days. The half-life for elimination is in the range of 10 to 30 h.

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