Oxcarbazepine

Comment

Adjunctive therapy or monotherapy of partial and secondary generalized seizures. Better tolerated and fewer interactions than carbamazepine. Efficacy spectrum restricted to partial epilepsies -- may be useful to treat primary generalized tonic–clonic seizures not associated with absence and myoclonic seizures, but not really encouraged. Higher incidence of hyponatraemia compared with carbamazepine. Interaction with oral contraceptives

FDA indication

Partial seizure, Monotherapy; 4yo and up
Partial seizure; Adjunct; 2yo and up

Mechanism

OXC and its derivative MHD are both antiepileptogenic -- OXC is essentially completely metabolized to MHD, and so MHD is primarily responsible for the antiepileptogenic effect.

1. OXC and MHD block voltage-gated sodium channels - similar to that of phenytoin and carbamazepine, but MHD has a greater affinity for the inactivated state of the channel

2. MHD blocks N- and P-type calcium channels, unlike carbamazepine, which has a greater effect on L-type channels.

3. MHD increases hippocampal dopamine and serotonin levels -- of uncertain significance

Starting dose

300 mg/day. Titration rate of 300 mg/week. Usual maintenance adult dose is 900-1800 mg/day. For children, starting dosage can be 45 mg/kg/day, increased by 5 mg/kg/day weekly. Usual maintenance dose in children is 20-45 mg/kg/day. Side effects considerably worse for adults treated with 1800--2400 mg/day.

Dose frequency

Twice daily

Converting from CBZ to OXC

Overnight conversion is usually well tolerated, especially for patients taking carbamazepine doses of 800 mg/day or less, but many physicians favour a more gradual approach. A conversion ratio of CBZ to OXC of 1 : 1.5 is reasonable for initial carbamazepine doses of 800 mg/day or less, but a ratio of 1 : 1 or 1 : 1.25 is often better tolerated for higher initial CBZ doses. For dosing algorithms see Albani F, Bisulli F, Barzaghi M. et al. Multicentre observational study evaluating immediate and progressive switching from carbamazepine to oxcarbazepine in patients with epilepsy. Funct Neurol 2007; 22:111--115.

Because of their differing effects on the CYP enzyme systems, conversion to OXC from CBZ may result in de-induction and an increase in the serum concentration of inducible AEDs.

Serum levels

Not routinely done. Check serum sodium at baseline, after 1--2 months of therapy, and after large dose increases -- this will detect most significant drops in serum sodium, but is not required.

Check serum sodium levels for susceptible patients (e.g. those taking diuretics), or if symptoms possibly indicating hyponatraemia -- nausea, malaise, headache, lethargy, confusion. Elderly patients are more susceptible, children less. Consider vitamin D levels.

Important interactions

Enzyme-inducing AEDs reduce the serum levels of the active metabolite MHD.

Oxcarbazepine reduces the serum levels of steroid contraceptives.

MHD is a potent inducer for CYP2C19 (as is CBZ) at higher doses, oxcarbazepine probably does cause significant inhibition of CYP2C19, with consequent elevations of serum concentrations of phenobarbital and phenytoin.

Important side effects

Oxcarbazepine is less likely to cause a skin rash than carbamazepine.

Effects on Epilepsy/EEG

OXC may worsen preexisting seizures, or cause new seizure types, and/or worsen the EEG following introduction of OXC monotherapy. EEG changes are primarily characterized by new onset of generalized epileptiform activity not reported on the initial baseline EEG. See, for example, Vendrame M, "Aggravation of seizures and/or EEG features in children treated with oxcarbazepine monotherapy", Epilepsia. 2007 Nov;48(11):2116-20.

Hyponatraemia

Dose-dependent, more common in elderly -- more problematic for OXC than CBZ. No fatal cases of CBZ- or OXC-induced hyponatraemia have been reported. If asymptomatic, I prefer Na to be 130 or higher. If clinical sx -- HA, nausea, fatigue, confusion -- then I reduce the dose; other meds incl SSRIs may worsen this, as well. See Van Amelsvoort, T., Bakshi, R., Devaux, C. B., & Schwabe, S. (1994). Hyponatremia associated with carbamazepine and oxcarbazepine therapy: a review. Epilepsia, 35(1), 181--188.
Hyponatremia usually occurs within the first 3 months of therapy, but may happen later if the dose is increased. Hyponatremia could cause an increase in seizures when serum levels fall below 125 mEq/L.