Serum Perampanel Levels in Adult Epilepsy Patients With Normal Liver Function: A Case Series at Ochsner Epilepsy Center

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Rationale

Perampanel (PER) is a relatively new anti-seizure medication that received FDA approval in 2012. It is a non-competitive AMPA glutamate receptor antagonist indicated for the treatment of partial-onset seizures, and as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients with epilepsy.

After oral administration, PER is absorbed rapidly and completely. It is metabolized by the cytochrome CYP3A4 and/or CYP3A5 primary oxidation and by sequential glucuronidation.

None of the PER metabolites are pharmacologically active.

Methods

We retrospectively reviewed 10 adult patients (age range 20-77 yrs) with normal liver function (based on liver function who were treated with PER and underwent testing for serum levels in the past 3 years at the Ochsner Epilepsy Center. We reviewed patient's serum levels of PER at corresponding doses, changes in seizure frequency, side effects at respective doses, and use of concomitant medications.

Results

Twenty-five blood levels in 10 patients were available for the analysis. The study included 7 females and 3 males. Ages ranged 20-77 years. Types of epilepsy included frontal lobe epilepsy (4), temporal lobe epilepsy (2), Lennox-Gastaut syndrome (LGS) (1), Idiopathic generalized epilepsy (1) and unclassified epilepsy (2).

Side effects reported to be associated with included forgetfulness, somnolence, behavioral outbursts, weight gain, irritability, intermittent dizziness, and weight gain. These diminished with reduction in dose or discontinuation. One of the two patients with >1000 ug/L reported behavioral outbursts and intermittent dizziness.

Concomitant medications included eslicarbazepine acetate, lacosamide, lamotrigine, levetiracetam, clobazam, brivaracetam, topiramate, vigabatrin, zonisamide, and EPIDIOLEX®.

	N	Average dose in mg	Dose range in mg	Average serum level in ug/L	Serum level range in ug/L
No seizure control	8	9	2-16	353	130-620
	2	13	12-16	>1000	>1000
>50% reduction in seizure frequency	1	7.5	6-8	242	130-290
100% seizure control	1	8	8	445	430-460
Side effects	3	12	8-16	476	280-620
	1	14	12-16	>1000	>1000

Conclusions

In prior studies, PER plasma concentrations increased in direct proportion to dose which aids the prediction of the effects of dose titration.

In one study, 21/76 Japanese patients aged 12 and older responded with ≥50% reduction of seizure frequency from baseline, and their mean serum PER concentration was 450 ng/mL (range: 85–1500).

In the patients who responded to PER in clinical trials, concentrations have ranged from 180 to 980 µg/L. This represents the current putative reference range.

In our study PER had a wide range of active serum levels, 130 to >1000 ug/L in patients who did not respond; 130-460 ug/L in responders

Individual factors may explain the large variation in steady state blood levels across patients.

We propose that blood level monitoring may be valuable for maintaining perceived therapeutic levels and guiding effective dose. Future systematic pharmacokinetic studies are needed to better understand a therapeutic range for PER.

References

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