Poster

[P26-1] P26-1: Anticonvulsant drugs

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[P26-1-5] Quinidine in epilepsy: TDM to improve therapy in migrant partial seizures of infancy

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Background

Migrating Partial Seizures of Infancy (MPSI) is an epileptic encephalopathy characterized by an early onset and focal seizures, associated to alterations in genes codifying ion channels such as KCNT1, and antiepileptic drug resistance.

Quinidine (QND) is an antiarrhythmic that modifies the potassium channel (KCN) conductance. Since KCNT1 is expressed in cardiomyocytes and neurones, QND was proposed as a new alternative treatment for patients with MPSI. QND adverse events, mainly prolonged QT segment, justify follow up with QND serum monitoring and ECG.

The objective of this work was to study QND plasma levels in one KCNT1 mutated patient, with the aim to propose a strategy for QND therapeutic monitoring in MPSI patients.

Methods

Our laboratory developed a HPLC-UV detection method to measure QND in serum samples (linearity 0.5-10 mcg/mL, LQ 0.5mcg/mL). Samples were drawn before next dose, after achieving steady-state. ECG was performed at least one week later after QND increase.

Results

A 4 years old girl with a KCNT1 mutation characterized using next generation sequencing with 25-30 seizures/day, prescribed with QND and topiramate (TPM) was studied.

During 2 months QND serum levels remained below 0.5 mcg/mL while QND dosis increased (400 to 640 mg/day) and TPM was reduced (200 to 100 mg/day). QND doses were further increased (560-720 mg/day) and its levels augmented to 1.0 mcg/mL when TPM dose was decreased from 100 to 20 mg/day. At QND 1000 mg/day serum level increased 60% when TPM was stopped. QND doses do not correlate with serum levels while TPM doses were above 100 mg/day.

Prolonged QT (0.48 and 0.51 s) was observed with 640 and 1000 mg/day of QND

Conclusions

Control of seizures was achieved at 1 mcg/mL (reference range:2-5 ug/ml). The results showed QND/TPM pharmacokinetic interaction. Intraindividual variability was evidenced in differences found at trough concentrations suggesting chronopharmacologic behavior of quinidine. The prolongation of QT segment corresponded to significant dose increases which were set in a short term. The information achieved suggests that individual therapeutic QND monitoring could be necessary to improve QND therapy in pediatric patients with KCNT1 mutation.