Pharmacokinetic variability of lacosamide in children and adolescents

Margrete Larsen Burns¹, Arton Baftiu², André Gottås³, Marina Nikaronova³, Jan B. Rasmussen³, Svein I. Johannessen¹,⁴, Cecilie Johannessen Landmark¹,³,⁴

1) Dept of Pharmacology, Oslo University Hospital, Norway 2) Programme for Pharmacy, Oslo Metropolitan University, Norway 3) The Danish Epilepsy Hospital, Filadelifa, Denmark 4) The National Center for Epilepsy, Oslo University Hospital, Norway

Background
Lacosamide is one of the most recently approved antiepileptic drugs (AEDs) with indication monotherapy and add-on therapy in adults, adolescents and children from 4 years with focal epilepsy. Serum concentration measurements are offered at some specialised laboratories.

Data on pharmacokinetic variability in young patients is scarce, since they are most often not included in clinical studies or exposed to drugs early after approval of new drugs (1).

The purpose of this study was to characterise pharmacokinetic variability of lacosamide in children and adolescents by use of therapeutic drug monitoring (TDM)-data.

Method
Retrospective anonymous data from the TDM-database at two national centers for epilepsy, Norway and Denmark were collected (2012-2017). The serum samples were drawn at steady-state, drug-fasting in the morning. The study was approved by the regional ethics committee.

Results and Discussion
The study included 144 patients aged 4-17 years (56 girls/88 boys). The daily dose of lacosamide varied from 100 to 600 mg/day. Mean serum concentration was 22 (range 4-53) μmol/L. The concentration/dose-ratio varied 12-fold, from 0.015 to 0.187 μmol/L/mg. When the children were grouped according to age, the variability was 4-fold in children <8 years (n=7), 7-fold in children 8-12 years (n=38), and 10-fold in adolescents 13-17 years (n=99). 84% of patients (n=123) had serum concentrations within the reference range (10-40 μmol/L), where we have previously shown that adults most often show efficacy (2).

We observed less variability in serum concentration than previously in adults (2), which may indicate closer follow-up in children.

Conclusion
• There were extensive pharmacokinetic variability of lacosamide among children and adolescents, but most patients had serum concentrations within the reference range.
• Lacosamide was mostly used in older children and adolescents.
• Implementation of TDM for new drugs contributes to characterisation of pharmacokinetic variability in special patient groups such as children and individualisation of pharmacotherapy.