Role of renal drug transporters on gabapentin renal excretion and influence of hyperglycemia on gabapentin population pharmacokinetics

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The effect of inflammatory diseases on drug pharmacokinetics (PK) and pharmacodynamics (PD) has been demonstrated by various studies. In type 2 diabetes (T2D), major complications are associated with inflammation due to chronic hyperglycemia and hyperglycemic memory. Chronic hyperglycemia can increase or decrease glomerular filtration rate depending on the severity of nephropathy and it can also alter the activity of drug transporters, which was already demonstrated for organic cation transporter 2 (OCT2). Gabapentin (GBP) is an anticonvulsant drug commonly used to treat diabetic neuropathy, and its elimination is primarily renal as unchanged drug. Some studies suggest GBP renal excretion is partially dependent on renal drug transporters, but it is not clear which ones might be involved. Thus, a clinical trial was conducted to evaluate the effect of hyperglycemia or T2D on GBP population pharmacokinetics (PopPk). Besides that, an in vitro study was conducted to evaluate the interaction of GBP with renal drug transporters expressed in HEK-293 cells. The data showed that diabetic patients had a reduction in systemic exposure to GBP, with no changes in renal excretion. PopPk showed that hyperglycaemia or T2D had no impact in distribution or excretion processes of GBP. Also, GBP had a strong affinity for renal transporters multidrug and toxin extrusion protein (MATE) 1 and 2K and organic zwitterion/cation transporter 1 (OCTN1) and a low affinity for organic cation transporter 2 (OCT2). In conclusion, T2D and hyperglycemia had no effect on GBP kinetic disposition, and it is suggested that MATEs and OCTN1 are involved in the excretion process of GBP, but OCT2 is not clinically relevant.

Biography

Carol has a Bachelors degreee in Pharmacy completed in 2014, and completed her PhD in 2019, in the field of Toxicology, from São Paulo University. She has experience with Clinical Pharmacokinetics and In Vitro Renal Transporters. She now works as a toxicologist pharmacist in the Toxicological Information and Assistance Cenrer in Santa Catarina, Brazil.

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