Bupropion/Hydroxybupropion Therapeutic Drug Monitoring: A Case of Elevated Hydroxybupropion Serum Levels in a Patient with Major Depressive Disorder and Chronic Kidney Disease

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Case

69-year-old male with a past medical history of coronary artery disease, chronic kidney disease stage 3, major depressive disorder, hospitalized for orthotopic heart transplantation. Hospital course was complicated by encephalopathy, acute kidney injury, and cardiac arrest requiring cardioversion.

69 y/o male hospitalized for heart transplant.

CL psychiatry was consulted during the hospitalization and recommended continuing his home antidepressant medications of vortioxetine 15mg daily and bupropion extended-release 300mg daily. He was also referred to the Medically Complex Psychiatry Clinic.

Continued home vortioxetine/bupropion.

At his intake clinic visit, he denied any active symptoms of MDD or encephalopathy. Reported MDD in remission for decades, historically aggravated by heavy alcohol use. Expressed desire to downtitrate antidepressant medications due to concerns of chronic kidney disease and polypharmacy.

In clinic, patient requested to stop antidepressants.

Creatinine clearance was calculated to be 39mL/min, so serum levels of bupropion and hydroxybupropion were obtained. Bupropion level found to be 15ng/mL (normal range 10-100), and hydroxybupropion level was 1,730ng/mL (normal range 850-1500).

Bupropion level normal, metabolite very elevated.

Bupropion downtitration was thus initiated in 150mg increments, as well as eventual downtitration of vortioxetine in 5mg increments, both well-tolerated with no return of depressive symptoms.

Antidepressants downtitrated.

Background

- Bupropion has a unique mechanism of action, acting as a dopamine and norepinephrine reuptake inhibitor, with no direct action on serotonin receptors (Khan, 2015).
- It is metabolized by CYP2B6 into several metabolites, the most significant and active of which is hydroxybupropion.
- Hydroxybupropion has a longer half-life than bupropion, reaches higher concentrations, and is renally cleared with significantly reduced clearance in renal failure patients (Costa, 2019).

	Metabolism	Elimination Half-Life	Therapeutic Level	Toxic Level
Bupropion	Hepatic via cytochrome P450-2B6	11-14 hours	10-100 ng/mL	>400 ng/mL
Hydroxybupropion	Renally cleared	15-25 hours	850-1,500 ng/mL	>2,000 ng/mL

References

1. Khan SR et al (2016). Bupropion Hydrochloride. Profiles of drug substances, excipients, and related methodology, 41, 1–30.
2. Costa R et al (2019). Pharmacokinetic and pharmacodynamic of bupropion: integrative overview of relevant clinical and forensic aspects. Drug metabolism reviews, 51(3), 293–313.
3. Nagler EV et al (2012), Antidepressants for depression in stage 3–5 chronic kidney disease: a systematic review of pharmacokinetics, efficacy and safety with recommendations by European Renal Best Practice (ERBP), Nephrology Dialysis Transplantation, 27(10), 3736–3745.

Discussion

- Bupropion therapeutic drug monitoring may be rarely used clinically but requires careful consideration in patients with CKD.
- While this patient had a normal bupropion level, the hydroxybupropion level was elevated and near the toxic range, consistent with normal hepatic function and significantly reduced renal function.
- Prior literature has advised dose reduction and raised concerns regarding the benefit of antidepressant use in patients with CKD (Nagler, 2012).