A Contribution to Emerging Evidence of Lithium Toxicity with GLP-1 Based Therapies

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Introduction

- Lithium remains a cornerstone treatment for bipolar disorder, with efficacy in mood stabilization and suicide risk reduction .
- GLP-1 receptor agonists are increasingly used for type 2 diabetes and weight management.
- Emerging reports suggest a potential association between GLP-1 based therapies and lithium toxicity, however no pharmacokinetic studies have been published regarding this.

Case

- Patient with bipolar II disorder, no prior lithium toxicity
- Normal renal function and no interacting medications
- Pre-tirzepatide:
  - Lithium 1.3 mEq/L on 1050 mg, asymptomatic
  - Decreased dose → **0.7 mEq/L on 900 mg**
- Post-tirzepatide:
  - Progressive weight loss
  - Lithium 1.2 mEq/L on 1050 mg
  - Emerging neurologic symptoms
- Toxicity phase:
  - Neurologic + GI symptoms
  - **Lithium 1.1 mEq/L on 900 mg**
  - Dose reduced to 600 mg
- Recovery:
  - Lithium 0.6 mEq/L on 600 mg
  - Resolution of symptoms

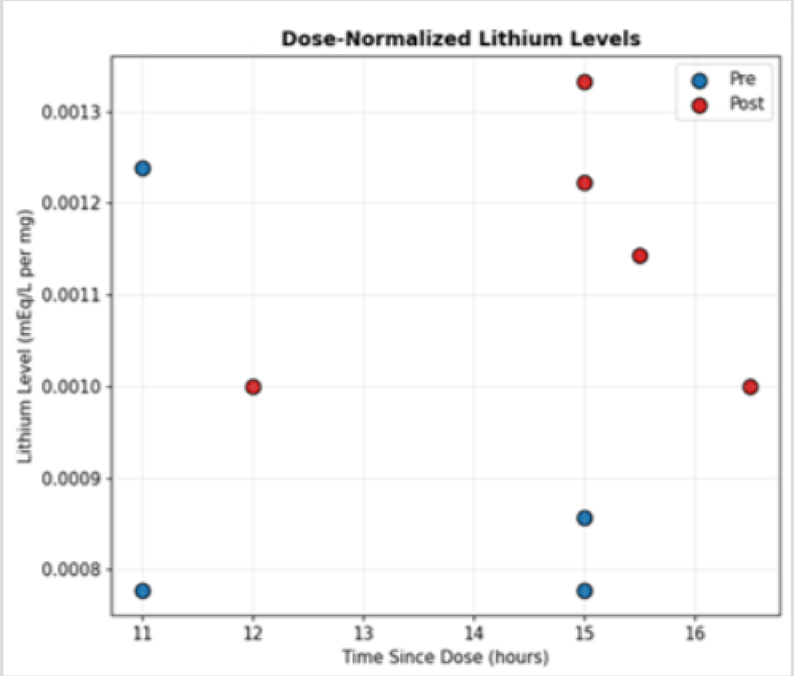

Figure: Dose-normalized analysis (lithium level/dosage) shows persistently increased lithium exposure post-tirzepatide initiation, based on time since last dose

Discussion

- Lithium has a **narrow therapeutic index**, with levels sensitive to volume status, renal function, sodium balance, and interacting medications.
- GLP-1–based therapies promote weight loss and delayed gastric emptying, with associated GI effects that may alter lithium exposure
- In this case, renal function remained stable, ruling out a common cause.
- An underappreciated variable in lithium dosing is time since last dose.
- Higher lithium exposure was observed after tirzepatide initiation **accounting for dose and timing of measurement.**
- Symptoms resolved with lithium dose reduction, despite continued tirzepatide administration, minimizing likelihood of direct adverse effect from tirzepatide.
- Potential mechanisms include delayed gastric emptying, weight loss, and subtle volume shifts, though not fully understood.
- The temporal association and similar reports with other GLP-1 agents suggest a possible class effect.

References

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Conclusion

This case adds to growing evidence that GLP-1 receptor agonists may increase lithium exposure through gastrointestinal effects. Clinicians should consider closer monitoring when co-prescribing.