

ECHO IDAHO



ECHO Idaho: Behavioral Health in Primary Care

Medication Monitoring

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Disclosures

- Dr. Carlson, in the past, has provided consulting services for Alkermes & Heron Therapeutics.

Learning Objectives

- Understand minimum lab monitoring requirements for safe use of atypical antipsychotic agents
- Identify overlooked interactions that require monitoring of lithium & valproic acid derivatives
- Understand “Alert Fatigue”
- Identify strategies for practicing clinical pharmacotherapy in patient psychiatric medication monitoring

Atypical Antipsychotic Agents - Monitoring

- Body Mass Index and waist circumference (baseline, 1mo, 2mo, 3mo, 6mo & annually)
- A1c (baseline, 3mo & annually)
- Lipid panel (baseline, 3mo & annually)
- Glucose (baseline, 3mo & annually)

Atypical Antipsychotic Agents

- Drug Interactions:
 - Tramadol: increased seizure risk
 - SSRI/SNRI: increased risk for serotonin syndrome
 - Carbamazepine: co-administration of lurasidone is contraindicated
 - Other QTc prolongation medications (chlorpromazine, haloperidol, citalopram, escitalopram, azithromycin, ciprofloxacin, erythromycin, fluconazole, levofloxacin, methadone & ondansetron)
 - Valproic Acid: see later slide

Interaction Monograph & Alert Fatigue

- **Severity Level** (Major, Moderate or Minor)
- **Documentation Level** (Established, Probable, Suspected, Possible or Doubtful/Unknown)
- **Onset** (Delayed or Rapid)
- **Summary**
 - Effect
 - Mechanism
 - Management
 - Discussion (with references)

Lithium - Monitoring

- Renal function, including BUN and serum creatine (baseline, every 2 to 3 months during the first 6 months of treatment, then once a year in stable patients or as clinically indicated)
- Serum electrolytes (baseline, then periodically), serum calcium (baseline, 2 to 6 weeks after initiation, then every 6 to 12 months; repeat as clinically indicated)
- Thyroid (baseline, 1 to 2 times within the first 6 months of treatment, then once a year in stable patients or as clinically indicated)
- Beta-hCG pregnancy test for all females not known to be sterile (baseline)

Lithium - Monitoring (continued)

- ECG with rhythm strip (baseline for all patients over 40 years of age or if underlying cardiac risk factors, repeat as clinical indicated),
- CBC with differential (baseline, repeat as clinically indicated);
- Serum lithium levels (twice weekly until both patient's clinical status and levels are stable, then repeat levels every 1 to 3 months or as clinically indicated)
- Weight (baseline, then periodically)

Lithium

- Drug Interactions:
- Reference range :
 - Obtain levels twice weekly until both patient's clinical status and levels are stable then levels may be obtained no less than every 6 months (APA 2002).
 - Timing of serum samples: Draw trough just before next dose (8 to 12 hours after previous dose).
- Therapeutic levels:
 - Acute mania: 0.5 to 1.2 mEq/L (SI: 0.5 to 1.2 mmol/L) (APA 2002).
 - Maintenance: 0.6 to 1 mEq/L (SI: 0.6 to 1.0 mmol/L); a higher rate of relapse is described in subjects who are maintained at <0.6 mEq/L (SI: 0.6 mmol/L) (APA 2002).

Lithium (Continued)

- Toxic concentrations
 - >1.5 mEq/L (SI: >1.5 mmol/L): Early signs and symptoms of intoxication may include marked tremor, nausea, diarrhea, blurred vision, vertigo, confusion, and decreased deep tendon reflexes (APA 2002).
 - >2.5 mEq/L (SI: >2.5 mmol/L): Intoxication symptoms may progress to include severe neurological complications, seizures, coma, cardiac dysrhythmia, and permanent neurological impairment (APA 2002).
 - >3.5 mEq/L (SI: >3.5 mmol/L): Potentially lethal toxicity (Mitchell 2001).
 - Note: A 10% to 26% increase of a 12 hour level can be expected with once daily dosing compared to a 12 hour level checked of an equal dose that is given twice daily (Mitchell 2001; Singh 2011). (NSAIDS)

Valproic Acid and Derivatives - Monitoring

- Liver enzymes (at baseline and frequently during therapy especially during the first 6 months)
- CBC with platelets (baseline and periodic intervals)
- PT/PTT (especially prior to surgery), serum ammonia (with symptoms of lethargy, mental status change)
- Serum valproate levels
- Suicidality (eg, suicidal thoughts, depression, behavioral changes)
- Motor and cognitive function (for signs or symptoms of brain atrophy)

Valproic Acid and Derivatives

- Drug Interactions:
 - Olanzapine: increased risk of elevated LFTs & decrease of olanzapine concentration.
 - Quetiapine: increased risk of neutropenia and leukopenia.

Valproic Acid and Derivatives (cont)

- Reference range:
 - In general, trough concentrations should be used to assess adequacy of therapy; peak concentrations may also be drawn if clinically necessary (eg, concentration-related toxicity). Within 3 to 4 days of initiation or dose adjustment, trough concentrations should be drawn just before the next dose (CANMAT/ISBD [Yatham 2018]).
 - When 24-hour extended release tablets are administered at bedtime, levels drawn at least 18 hours post-dose have been suggested to provide an acceptable estimate of trough concentrations when levels timed closer to the next dose are inconvenient (eg, during outpatient monitoring) (Reed 2006).
 - Additional patient-specific factors must be taken into consideration when interpreting drug levels, including indication, age, clinical response, pregnancy status, adherence, comorbidities, adverse effects, and concomitant medications (Patsalos 2018).

Valproic Acid and Derivatives (cont)

- Valproic acid, total:
- Therapeutic:
 - Epilepsy: 50 to 100 mcg/mL (SI: 350 to 700 micromole/L); although seizure control may improve at levels >100 mcg/mL (SI: 700 micromole/L), toxicity may occur at levels of 100 to 150 mcg/mL (SI: 700 to 1,040 micromole/L)
 - Mania: 50 to 125 mcg/mL (SI: 350 to 875 micromole/L); lower levels up to 90 mcg/mL (624 micromole/L) have been suggested in the elderly (Chen 1999).
- Valproic acid, free:
 - Therapeutic: 5 to 15 mcg/mL (Smetana 2016)

Key Points

- If you start an atypical, begin tracking BMI, A1c & Lipids
- Good interaction monographs can be your best tool for evaluating the evidence
- QTc prolongation additive effects & EKG monitoring

References

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