Psychotropic Medication: Part 3

SOLUTION·S
www.solution-s.ca

Mood Stabilizers

Terry Broda, RN(EC), BScN, NPHC,CDDN
Elizabeth Kacew, RN(EC), MScN, NP-PHC

September 29, 2014

MOOD STABILIZERS

Mood disorders:

- Defined by presence of mood episodes
- Combination of symptoms comprising a predominant mood state that is abnormal in quality and duration:
  - Major depressive
  - Manic
  - Mixed
  - Hypomanic

MOOD STABILIZERS

Types of mood disorders include:

- Depressive
  - Major depressive disorder, dysthymia
- Bipolar
  - Bipolar I/II, cyclothymiacs
- Secondary to substances/medication
  - Vascular, infectious, neoplastic, degenerative drugs, autoimmune, endocrine/metabolic

MOOD STABILIZERS

Recent epidemiological studies focused on community samples and found rates of **mood disorders** from **3% to 8.1%.**

Mood disorders are found to be **more prevalent** than psychotic disorders or anxiety disorders.

(Antonacci & Attiah, 2008)

MOOD STABILIZERS

Carbolith, Duralith	➢ Lithium
Depakene*, Epival*, Depakote*	➢ Valproic Acid*, Divalproex* ➢ Sodium Valproate*
Tegretol* Trileptal* Lamictal* Neurontin* Topamax* *used as AEDs also	➢ Carbamazepine* ➢ Oxcarbazepine* ➢ Lamotrigine* ➢ Gabapentin* ➢ Topiramate*

MOOD STABILIZERS:

Antipsychotics used as mood stabilizers

• Zyprexa	➢ Olanzapine
• Risperidone	➢ Risperdal
• Quetiapine	➢ Seroquel
• Clozapine	➢ Clozaril
• Paliperidone	➢ Invega
• Aripiprazole	➢ Abilify
• Olanzapine/Fluoxetine	➢ Symbax (not in CANADA)

MOODSTABILIZERS
Indications

- **Bipolar disorder**
- **Acute mania**
- Increases SSRI efficacy in depression & OCD
- Organic brain disorders with affective symptoms
- Other behavioural concerns: aggression, impulsivity, gambling (Li), anorexia
- Migraine cluster headaches
- Anticonvulsant

MOOD STABILIZERS
Side effects

- dry mouth
- drooling
- increased gum growth
- constipation
- diarrhea
- nausea/vomiting
- increased thirst
- increased appetite
- abdominal pain
- weight gain/weight loss
- increased urination
- difficult urination
- urinary incontinence
- fecal incontinence
- restlessness
- nervousness
- dizziness
- slurred speech
- tremor
- fainting
- impaired memory
- headaches
- confusion
- seizures
- abnormal gait
- leaning to side
- rigidity
- abnormal posturing/movements

MOOD STABILIZERS
Side effects

- eye movements
- change in facial expression
- acne
- sun burn
- itching
- swelling
- bruising
- skin rash/hives
- trouble breathing
- cough
- nasal congestion
- difficulty swallowing
- difficulty falling asleep
- increased sleep
- daytime drowsiness
- interrupted sleep
- nightmares
- irritability
- withdrawn
- sweating
- hair loss/gain
- menstrual changes
- breast D/C

MOOD STABILIZERS
Current Problems

- Limited efficacy
- Toxicity
- Side effects: renal, thyroid, hematological, hepatic
- Monitoring
- Interactions
- Teratogenicity
- Weight gain

Lithium

- **Therapeutic Range**
  - 0.6 – 1.2 mEq/L
- Clearance predominantly through kidneys (95%)
- Dosing adjusted based on renal function
  - Individuals with chronic renal insufficiency must be closely monitored
  - Re-absorption of lithium is increased and toxicity more likely in patients who are hyponatremic or volume depleted (ex. vomiting, diarrhea, diuretics)
- **Half life**
  - 12 to 27 hours
  - Increases to 36 hours in elderly persons (**renal function)
  - May be considered longer with long-term lithium use (up to 58 hours after one year of therapy)

Side Effects of Lithium

Renal Effects
- Polyuria
- Nephritis

GI symptoms
- Diarrhea
- Nausea or vomiting
- Dehydration & dry mouth
- Abdominal discomfort

Motor Symptoms
- Mild tremor or muscle contractions
- Muscle weakness
- Lack of coordination
- Ataxia
- Difficulty articulating speech

CNS symptoms
- Somnolence
- Decreased concentration or memory
- Tremor
- Seizures
- Coma

Cardiac side effects
- Arrhythmias

Dermatological reactions
- Dermatitis, psoriasis
- Dry brittle hair or hair loss

Starting Li+ therapy

SE to observe:

- Fatigue, weakness, slurred speech
- Hand tremor, N &V, thirst, polyuria
- Edema of hands & feet, abdomen or face.

Which SE usually disappear within a week?

- Fatigue, N & V.

Which ones persist for longer?

- Thirst, polyuria, hand tremor

Which are signs of Li+ toxicity ?

- Slurred speech, diarrhea, vomiting, increased hand tremors, fatigue, muscle weakness, ataxia

Diet & Li+

- No restrictions but must maintain same level of salt intake during therapy
- If salt intake increased, then Li+ will be excreted faster : MANIA
- If salt intake is decreased (gastro, vomiting, increased exercise), then Li+ will be excreted more slowly : TOXICITY

Lithium Toxicity

- **Closely related to concentration of lithium in the blood**
  - Serum concentrations above 1.5 mmol/L
- **Preceded by appearance/aggravation of:**
  - Sluggishness, drowsiness, lethargy, coarse hand tremor or muscle twitching, loss of appetite, vomiting and diarrhea

****Repeated episodes of lithium toxicity can cause kidney damage**

Considerations

- Half-life: 8 to 35 hours, can give one dose/day, HS or with a meal (increased compliance & less toxic to kidneys)
- Half-life increases with duration of Tx
  (up to 58 hrs after one yr!)
- Dividing doses can decrease certain SE
  (tremors, urinary frequency, nausea)
- Acute mania: 900-2400/day (0.8-1.2mmol/L)
- Maintenance dose: 400-1200/day (0.6-1mmol/L)

Considerations

- Elimination: 95% by kidneys so adequate renal function is essential to avoid toxicity: need to verify eGFR prior to tx
- If creatinine clearance 10-15ml/min, use 50-75% of the standard dose
- If creatinine clearance <10ml/min, use 25-50% of the standard dose

Considerations when initiating treatment

Verify past medical hx & family hx for:

- Other medications (do not take with NSAIDs, ACE-Is, ARBs, CCBs, VPA, CBZ, PHT, SSRIs, haloperidol, clozapine, & certain antibx) may increase risk of Li toxicity or neurotoxicity
- Thyroid function
- Cardiovascular disorders
- Monitor levels 5 days after start of Tx, then weekly X2, then when dose changed or new Rx added

Considerations

Labwork at start of Tx & every admission to H:

- Electrolytes, fasting blood glucose,
- Hb, Hct, CBC & differential,
- Thyroid function,
- Creatinine,
- Ca, phosphorus,
- ECG for patients > 40yrs, or w/ hx heart disease
- Lithium levels
- Pregnancy test

Considerations

- Labwork every 3 months & then q.6 months:
  - Hb, Hct, CBC & differential, thyroid function
- At 6-12 months: creatinine (eGFR), parathyroid & TSH
- At 1-2 years: Calcium, phosphorus
- At 5 years: ECG for patients > 40 years, or w/ hx heart disease

Considerations

- **DO NOT** decrease or drastically alter caffeine intake
- **DO NOT TAKE** morning dose of Lithium before blood work for Li levels (needs to be 9-13 hrs: trough levels)
- **DO NOT CHEW** long acting formulation

Indications

- **Bipolar disorder(CBZ, VPA, LMG)**
- **Acute Mania (CBZ, VPA)**
- Anticonvulsants
- Chronic pain(CBZ, GBP, VPA, LMG, TPX)
- Migraines (VPA, TPX, GBP, LMG)
- CB (DEMENTIA, DD) (CBZ, VPA, TPX)
- Borderline Personality (CBZ, TPX, VPA, LMG)
- Add-on tx for anxiety dx, paranoia, substance abuse

Considerations

CBZ:

- Auto-metabolizer ()
- Induction of other Rx's, so check other AED levels before starting CBZ
- Anticholinergic SE
- ATTENTION: pts of Asian ancestry w/ allele for HLA-B*1502 have an increased risk of serious dermatological reaction (SJS)
- ⇩ therapeutic range for Sz dx , ⇧ for bipolar dx

Considerations

VPA: Inhibition of other Rx (CYP-450 enzymes)

Do not give w/ clonazepam as this may induce **absence sz**

LMG: ATTENTION: increased risk of severe dermatological reaction (SJS), esp. w/⇧ doses,⇧ titration & w/ + VPA

TPX

- Lower doses in elderly & those w/ renal or hepatic impairment
- Increased risk of renal calculi, hyperthermia & glaucoma
- ADR paresthesia (25%), SE can include wt. loss
- Cognitive effects (r/t dose), may ⇧ aggression/psychosis

GBP

- Eliminated by kidneys so adjust dosage in the elderly & if renal impairment

Comparison of AEDs

	Carbamazepine (CBZ)	Oxcarbazepine (OXC)	Valproic Acid/Divalproex (VPA/DVA)	Gabapentin (GBP)	Topiramate (TPM)
Doses	300-1600mg/day BID-TID dosing *available in CR form	600-1200mg/day in divided doses	750-3000mg/day BID-TID dosing	900-3600mg/day TID dosing	50-400mg/day BID dosing
Meta-bolism	Liver & P-gp * induces own metabolism	Liver * DOES NOT induce own metabolism	Liver	Not metabolized, Eliminated by renal excretion	P-gp, (70% is eliminated unchanged in urine)
Drug levels	17-54 µmol/L **(Cdn)** 4-12 mcg/ml **(USA)** * Frith: 3wks after Rx started, Verani: initially 2 levels taken 4 wks apart & both agree with testing 5d after Δ dose or +/- other Rx , may need to check other Rx levels if CBZ added	Not required	350-800 µmol/L **(Cdn)** 50-115 mcg/ml **(USA)** *initially 2 levels to establish dosage, 3-5d after Rx started & 5d after Δ dose or +/- other Rx (Verani); Frith recommends only if toxicity or non-compliance suspected, & DeLeon q.6 months thereafter	Not required	Not required
W/U	1. CBC, plats & diff 2. E-, BUN, sCr 3. LFTs 4. TSH 5. ECG (>45yrs) 6. BMD 7. r/o pregnancy	1. E- 2. Cr	1. **CBC, plats & diff** 2. **LFTs** 3. **Lipid profile (total, HDL & TG)** 4. **-: wt & BMI & r/o pregnancy** 5. **Consider serum testosterone in young -** 6. **BMD** 7. **Serum amylase & lipase**	BUN & sCr	Baseline serum bicarbonate BUN & sCr
F/U	Repeat #1, 2, & 3 monthly X 3 months, then annually BMD if risk factors for osteopenia ****Increased risk of SJS in certain Asian populations.**	Na+ levels when suspected hyponatremia.	Repeat #1 &2 monthly X2, then 2-3X/yr (Verani).. Repeat #1 &2 monthly X8, then annually (Frith). Repeat #3 &4 q.3 months X4, then annually. Test #5 if s/s of menstrual irregularities or hyperandrogenism; also test prolactin, LH & TSH, & for insulin resistance & HTN. Ammonia levels if lethargy & Δ LOC.	LH & TSH sCr if renal toxicity suspected	Periodic serum bicarbonate; sCr if renal toxicity suspected (risk of kidney stones)

www.solution-s.ca

Comparison of AEDs

	Lamotrigine (LTG)	Levitiracetam (LEV)	Zonisamide (ZNS) (*sulfa Rx)	Tiagabine (TGB)	Phenobarbital (PB)	Phenytoin (PHT)
Doses	100-500mg/day BID dosing	1000-3000 mg/day BID dosing	100-600mg/day in single or BID dosing	32-56mg/day BID-QID dosing	15-180mg/day in single or divided doses	300-400mg/day in single or divided doses
Meta-bolism	Liver (NO effect on P450 Enzymes)	Not metabolized, Eliminated by renal excretion (66% eliminated unchanged in urine)	Liver	Liver	Liver	Liver
Drug levels	Not required	Not required	Not required	Not required	65-150 µmol/L **(Cdn)** 20-40 mcg/ml **(USA)**	40-80 µmol/L **(Cdn)** 10-20 mcg/ml **(USA)**
W/U	Skin exam CBC & diff, LFTs, E-, sCr, r/o pregnancy	CBC, plats & diff, sCr	CBC & diff, LFTs, sCr		CBC & diff, LFTs	CBC & diff, LFTs, folate?
F/U	CBC, LFTs annually ****monitor closely for SJS in first 2 months**	CBC & diff, sCr annually	CBC & diff, LFTs, sCr annually (risk of kidney stones)	none	CBC & diff, LFTs annually. BMD/Vit D	CBC & diff, LFTs, folate annually. BMD/Vit D

Virani, A., Bezchlibnyk-Butler, K., & Jeffries, J., *Clinical Handbook of Psychotropic Drugs*, (2012); Saskatoon City Hospital, *Rx Files Drug Comparison Charts*, (2008), Bhaumik, S. & Branford, D.,*The Frith Prescribing Guidelines for Adults with Intellectual Disabilities*, (2008), DeLeon, J., *A Practitioner's Guide to Prescribing Antiepileptics and Mood Stabilizers for Adults with Intellectual Disabilities (2012).*

www.solution-s.ca

Medication	Systemic/physical Effects	CNS Effects
Clonazepam (Rivotril)	Drooling *Rare:* Rash Paradoxical reaction Thrombocytopenia Depression	Sedation, dizziness Risk of aspiration Paradoxical reaction: disinhibition ↓ Concentration Anterograde amnesia Ataxia Nystagmus
Carbamazepine (Tegretol) ***CR tab < effects GI & CNS**	Rash/ Pruritis/urticaria ✓ Fever/sore throat d/t ↓ WBC ↓ Vit D *Rare:* Aplasic anemia, ↑ LFTs (GGT/ALK), Hyponatremia (SIADH) Cardiac abnormalities ↓ T3/T4/Vit K Alopecia, visual disturbances.	N & V Diplopia Ataxia Sedation, dizziness Dyskinesia Nystagmus

Medication	Systemic/physical Effects	CNS Effects
Valproic Acid (Depakene) *(VPA > GI SE)* **Divalproex (Epival)**	Alopecia Abdominal cramps Hyperammoniemia Menstrual irregularities *Rare:* ↓ platelets & WBC Hepatotoxicity Pancreatitis Carnitine deficiency ATTENTION : PCOS Obesity (esp in ♀) *SJS w/ Lamotrigine	**Sedation, fatigue dizziness, ataxia** **N & V** Confusion Headache Tremors
Gabapentin (Neurontin)	Edema Weight gain Rash Behavioral Δ, irritability (children) ↓ WBC Decreased platelets(rare) ECG Δ (rare)	**Lethargy, fatigue dizziness, ataxia** Headache N & V Diplopia Tremors Speech difficulties/slurring

Medication	Systemic/physical Effects	CNS Effects
Lamotrigine (Lamictal)	Rash (1st month : gen. red morbilliform) Abdominal discomfort Alopecia *Rare:* SJS & toxic epidermal necrolysis Hepatotoxicity Tics (chldren)	Dizziness, ataxia N & V Asthenia Headache Fatigue Blurry vision, diplopia
Topiramate (Topamax)	Diarrhea Weight loss Kidney stones Glaucoma Rare: ↑ LFTs	Fatigue Headache Dizziness, ataxia Agitation Behavioral Δ Paresthesias (fingers, toes) Cognitive deficits (memory, concentration, word-finding)

Considerations

solution-s

- Anticholinergic effects increase in combination with other Rx
- Monitor for fever, sore throat, bruising or bleeding
- Monitor skin for SJS
- Monitor for other SE or signs of toxicity:
  - N & V, ataxia, confusion

Considerations

For CBZ:

- DO NOT TAKE with grapefruit
- But, do take w/ food to ⇩GI upset
- DO NOT ADMINISTER susp. with other Rx in liquid format : this will form an insoluble precipitate

For VPA:

- DO NOT TAKE ASA or bismuth (risk of toxicity) (acetaminophen/ibuprofen may be better choice)
- Do not take liquid form with soda/carbonated beverage: may cause irritation in the mouth

Considerations

- **DO NOT TAKE** morning dose before blood work for drug levels (needs to be 8 to12 hours, trough levels)
- **DO NOT CHEW** enteric-coated tabs or long acting formulation (VPA, Tegretol CR)

Responsibilities of the staff & caregivers

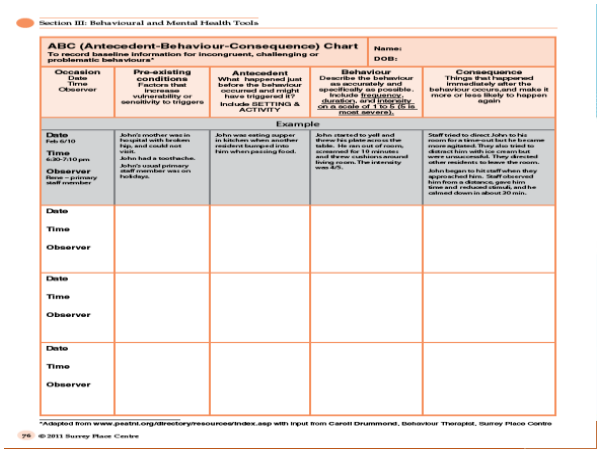
- Safe storage
- Safe administration, limit errors
- Follow-up of medication efficacy
- Monitoring of side effects
- Asking questions & observation!

Questions (for caregiver to ask MD)

- Why do you recommend this treatment?
- How can we tell if things are getting better?
- What are the risks of this treatment?
- What should we do if side effects occur?
- What information do you need for the next appt.?
- When should we call you?
- Are there any checklists or scales that we could use?
- Are there any lab tests that need to be done?
- When should we schedule another appointment?

Useful Tools!

- A-B-C sheets
- Scatterplot
- Pain checklist
- MAR medication sheets & PRN sheet
- Follow up form for MD
- Observations of SE & movements
- Medication history



Section III: Behavioural and Mental Health Tools

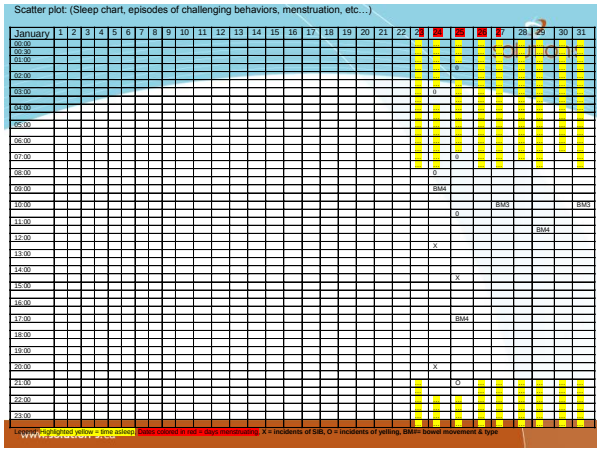
ABC (Antecedent-Behaviour-Consequence) Chart
To record baseline information for incongruent, challenging or problematic behaviours*

Name:
DOB:

Occasion Date Time Observer	Pre-existing conditions Factors that increase vulnerability or sensitivity to triggers	Antecedent What happened just before the behaviour occurred and might have triggered it? Include SETTING & ACTIVITY	Behaviour Describe the behaviour as objectively and specifically as possible. Include frequency, duration, and intensity on a scale of 1 to 5 (5 is most severe).	Consequence Things that happened immediately after the behaviour occurred, and make it more or less likely to happen again
Example				
Date Feb 6/10 Time 4:30-7:10 pm Observer Rene – primary staff member	John's mother was in hospital with broken hip, and could not visit. John had a toothache. John's usual primary staff member was on holidays.	John was eating supper in kitchen when another resident bumped into him when passing food.	John started to yell and throw things around in the room. No physical harm. Continued for 10 minutes and threw cushions around living room. The intensity was 4/5.	Staff tried to direct John to his room for a time out. This became a power struggle. They also tried to distract him with ice cream but were unsuccessful. They directed other residents to leave the room. John began to hit staff when they approached him. Staff observed him from a distance and he calmed down in about 30 min.
Date Time Observer				
Date Time Observer				
Date Time Observer				

*Adapted from www.psatnl.org/directory/resources/index.asp with input from Carol Drummond, Behaviour Therapist, Surrey Place Centre

76 © 2011 Surrey Place Centre



Individualized

solution-s

SE/hr	D/E/N	D/E/N	D/E/N	D/E/N	D/E/N	D/E/N	D/E/N
Blurry vision							
Congestion							
Dry mouth							
Abnormal movements							
Rigidity							
Dizziness							
Falls							
Constipation							
Urinary retention							
Vomitting							

Medication

- Safe storage
- Safe administration, limit errors
- Name & photos well-indicated
- Clear & precise documentation :
  - Regular Rx
  - PRNs
- Effects of the PRNs well-documented

THANK YOU!

29-2450 Lancaster
Ottawa, Ontario K1B 5N3
T 613 249-8593
F 613 249-0198
info@solution-s.ca
www.solution-s.ca