

Psychotropic Medication

SOLUTION:s
www.solution-s.ca

Part 3: Mood Stabilizers

with Terry Broda

MOOD STABILIZERS

SOLUTION:s

| | |
|-------------------------------|---|
| Carbolith, Duralith | ➤ Lithium |
| Depakene*, Epival*, Depakote* | ➤ Valproic Acid, Divalproex ➤ Sodium Valproate |
| Tegretol* | ➤ Carbamazepine |
| Trileptal* | ➤ Oxcarbazepine |
| Lamictal* | ➤ Lamotrigine |
| Neurontin* | ➤ Gabapentine |
| Topamax* | ➤ Topiramate |

www.solution-s.ca

Indications

SOLUTION:s

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

www.solution-s.ca

Problems of Current Mood Stabilizers



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



www.solution-s.ca

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)

www.solution-s.ca

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

www.solution-s.ca

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

www.solution-s.ca

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

www.solution-s.ca

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 twitchings, loss of appetite, vomiting and diarrhea

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

www.solution-s.ca

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)

www.solution-s.ca

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

www.solution-s.ca

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

www.solution-s.ca

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

www.solution-s.ca

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 > 40yrs, or w/ hx heart disease

www.solution-s.ca

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

www.solution-s.ca

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

www.solution-s.ca

Considerations



CBZ:

- Auto-metabolizer (🍌)
- Induction of other Rx's
- Anticholinergic SE
- ATTENTION: pts w/ Asian ancestry w/ HLA-B*1502 + have increased risk of serious dermatological reaction (SJS)

www.solution-s.ca

Considerations



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

LMG: ATTENTION: increased risk of severe dermatological reaction, esp. w/ VPA

TPX

- Increased risk of renal calculi
- Increased risk of glaucoma
- Cognitive effects (dose dependant)

GBP

- Eliminated by kidneys, adjust dosage if renal impairment

www.solution-s.ca

| Comparison of AEDs | | | | | |
|--------------------|---|---|--|--|--|
| | Carbamazepine (CBZ) | Oxcarbazepine (OXC) | Valproic Acid/Divalproex (VPA/DVA) | Gabapentin (GBP) | Topiramate (TPM) |
| Doses | 300-1600mg/day BID-TID dosing | 600-1200mg/day in divided doses | 750-3000mg/day BID-TID dosing | 900-3600mg/day TID dosing | 50-400mg/day BID dosing |
| Meta-bolism | *available in CR form Liver & P-gp *induces own metabolism | Liver * DOES NOT induce own metabolism | Liver | Not metabolized, Eliminated by renal excretion | P-gp, (70% excreted unchanged in urine) |
| Drug levels | 17-54 µmol/L (C ₀) 4-12 mg/ml (USA) * (F ₀): 2 hrs after Rx started, V ₀ (A ₀): initially 2 levels taken 4 wks apart & both agree with testing 1st after a dose or +/- other Rx... may need to check other Rx levels if C ₀ added | Not required | 350-800 µmol/L (C ₀) 50-115 mg/ml (USA) *initially 2 levels to establish dosage, 3-5d after Rx started & 8d after a dose or +/- other Rx. V ₀ (A ₀): (F ₀) recommends only if toxicity or non-compliance suspected, & Delago q 6 months thereafter | Not required | Not required |
| W/U | 1. CBC, platelets & diff 2. E, BUN, sCr 3. LFTs 4. TSH 5. ECG (>45yrs) 6. BMD 7. /fo pregnancy | 1. E- 2. Cr | 1. CBC, platelets & diff 2. LFTs 3. Lipid profile (total, HDL & TG) 4. +/- wt & BMI & /fo 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 X3 months, then annually BMD if risk factors for osteopenia **increased risk of SIS in certain Asian populations. | Na+ levels when suspected hyponatremia. | Repeat #1 & 2 monthly X2, then 3-5x/yr (V ₀ (A ₀)). Repeat #1 & 2 monthly X6, then annually (F ₀). Repeat #3 & 4 q 3 months X6, then annually. Test #5 if 1/2 of pregnancy, 1/3 (G ₀ (A ₀)) or hyperandrogenism, abnormal protein, LH & TSH, & for insulin resistance & HTN. Ammonia levels if lethargy & a 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 (LTV) | Levetiracetam (LEV) | Zonisamide (ZNS) (Trade: Zov | Topiramate (TPM) | 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 (65% excreted unchanged in urine) | Liver | Liver | Liver | Liver |
| Drug levels | Not required | Not required | Not required | 65-150 µmol/L (C ₀) 20-40 mg/ml (USA) | 40-80 µmol/L (C ₀) 10-20 mg/ml (USA) | 40-80 µmol/L (C ₀) 10-20 mg/ml (USA) |
| W/U | Skin exam CBC & diff, LFTs, E, sCr, /fo pregnancy | CBC, platelets & diff, sCr | CBC & diff, LFTs, sCr | CBC & diff, LFTs | CBC & diff, LFTs, sCr if renal toxicity | CBC & diff, LFTs, sCr if renal toxicity |
| F/U | CBC, LFTs annually **monitor closely for SIS in first 2 months | CBC & diff, sCr annually | CBC & diff, LFTs, sCr annually (risk of kidney stones) | none | CBC & diff, LFTs annually, BMD/xyt D | CBC & diff, LFTs, sCr annually, BMD/xyt D |

Virani, A., Beschta-Blyk-Butler, K., & Jeffries, J., *Clinical Handbook of Psychotropic Drugs*, (2012), Saskatoon City Hospital, Rx Files Drug Comparison Charts, (2008), Bhaumik, S. & Branford, D., *The First 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 <u>Rare:</u> Rash Paradoxical reaction Thrombocytopenia Depression | Sedation, dizziness Risk of aspiration Paradoxical reaction: disinhibition ↓ concentration Anterograde amnesia Ataxia Nystagmus |
| | Pruritis/urticaria ↓ WBC, ↓ Vit D <u>Rare:</u> Aplastic anemia, ↑ LFTs (GGT/ALK), Hyponatremia (SIADH) Cardiac abnormalities ↓ T3/T4/Vit K Alopecia, visual disturbances, Osteomalacia | N & V Diplopia Ataxia Sedation, dizziness Dyskinesia Nystagmus |

*CR tab < effects GI & CNS

| Medication | Systemic/physical Effects | CNS Effects |
|--|--|--|
| Valproic Acid (Depakene) (VPA > GI SE) | Alopecia Abdominal cramps Hyperammonemia Menstrual irregularities <i>Rare:</i> ↓ platelets & WBC Hepatotoxicity Pancreatitis | Sedation, fatigue dizziness, ataxia N & V Confusion Headache Tremors |
| Divalproex (Epival) | Carnitine deficiency ATTENTION: PCOS Obesity (esp in ♀) *SJS w/ Lamotrigine | |
| 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 <i>Rare:</i> SJS & toxic epidermal necrolysis Hepatotoxicity Tics (children) | 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) |

| Medication | Systemic/physical Effects | CNS Effects |
|--------------------------------|---|--|
| Phenobarbital | Rash Sleep disturbance ↓ Vit D & K <i>Rare:</i> blood dyscrasias, liver toxicity | Sedation, dizziness, ataxia Nystagmus ↓ concentration & cognition behavioral Δ, irritability (children) |
| Phenytoin (Dilantin) | Hirsutism Acne Gingival hyperplasia (50%) ↓ folate/T4/Vitamins D & K Rash Osteomalacia ↑ liver function tests blood dyscrasias | Ataxia, dizziness Nystagmus ↓ concentration Sedation Dyskinesia, tremor Arrhythmia N & V, diarrhea |
| Ethosuximide (Zarontin) | Anorexia <i>Rare:</i> Rash (SJS), blood dyscrasias behavioral Δ (children) | Sedation, dizziness <i>Hiccups</i> Headache N & V, diarrhea |

Considerations



- 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

www.solution-s.ca

Considerations



For CBZ:

- DO NOT TAKE with grapefruit
- 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

www.solution-s.ca

Considerations



- **DO NOT TAKE** morning dose before blood
work for drug levels (needs to be 8 to 12
hours, trough levels)
- **DO NOT CHEW** enteric-coated tabs or long
acting formulation (VPA, Tegretol CR)

www.solution-s.ca

Responsibilities of the staff & caregivers



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

www.solution-s.ca

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 appt.?

www.solution-s.ca

Useful Tools!



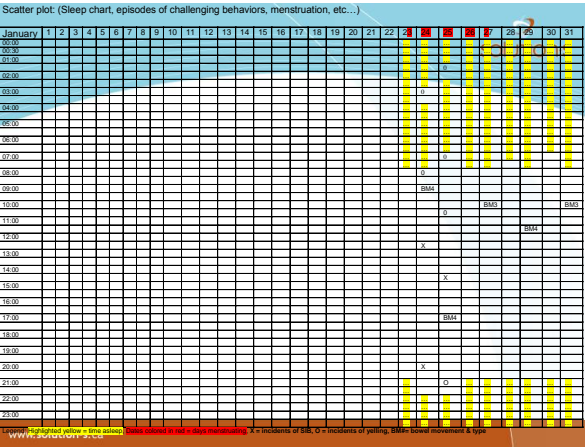
- A-B-C sheets
- Scatterplot
- Pain checklist
- MAR medication sheets & PRN sheet
- Follow up form for MD
- Observations of SE & movements
- Medication history

www.solution-s.ca

Section III: Behavioural and Mental Health Tools

| ABC (Antecedent-Behaviour-Consequence) Chart To record baseline information for inconspicuous, challenging or problematic behaviour. | | | | |
|---|--|--|---|---|
| Name: _____ | | | | DOB: _____ |
| Occasion (Date, Time, Context) | Pre-existing conditions (Factors that increase vulnerability or sensitivity to triggers) | Antecedent (What happened just before the behaviour occurred or what have triggered it? Include ACTIVITY & SITUATION) | Behaviour (Describe the behaviour as accurately and specifically as possible. Include frequency, duration, or intensity, if most severe) | Consequence (Things that happened immediately after the behaviour. Specify what praise or loss likely to happen right) |
| Examples | | | | |
| Date: Feb 10/10 Time: 8:30-7:10 pm Observer: Mum (primary school teacher) | John's mother was in a heated with her boss. She was shouting and crying, and could not sleep. John had a headache. John used primary school teacher's backpack. | John was sitting opposite to his father when another student walked through the aisle. His mother was talking to him when passing fence. | John started to yell and threw his paper across the aisle. He was out of control, accompanied by 10 minutes and some middle-classed being seen. The intensity was 8/10. | Staff tried to direct John to the toilet for a bathroom but he had some severe equipment. They also tried to direct him away from the classroom and to the classroom. They directed other students to leave the room. John began to hit staff when they approached him. Staff observed him from a distance until he was calmed down to about 30 min. |
| Date | | | | |
| Time | | | | |
| Observer | | | | |
| Date | | | | |
| Time | | | | |
| Observer | | | | |
| Date | | | | |
| Time | | | | |
| Observer | | | | |

*Adapted from www.pbti.org.au/infocentre/resources/index.asp with input from Carol Drummond, Behaviour Therapist, Sunny Plains Centre
© 2011 Sunny Plains Centre



- Observational Pain checklist
- Medication administration records (MAR) & PRN sheets
- Follow-up forms for MD
- Medication history

www.solution-s.ca

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

www.solution-s.ca

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

www.solution-s.ca

Individualized



| 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 | | | | | | | |
| Vomiting | | | | | | | |

Medication



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

www.solution-s.ca

THANK YOU!



www.solution-s.ca



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