Management of Alcohol Withdrawal Syndrome in the ICU

Every patient with diagnosis of alcohol withdrawal syndrome in the ICUs at Flagler Hospital will be eligible for this protocol. As with any protocol, this protocol serves to provide evidence-based, comprehensive recommendations to guide our multidisciplinary team in patient care, with the expectation that expert practitioners will modify and customize as necessary to meet individual patient needs. This protocol is not intended to replace the practitioner's judgment; it is intended to provide guidance to the physician for the group of patients described in the protocol.

Baseline monitoring and interventions

- Monitor CMP, serum magnesium and serum phosphorus daily in AM x3 days.
- Give sodium chloride 0.9% IVPB + Thiamine 100 mg + Folic Acid 1 mg + oral multivitamins daily x3 days.
- Provide frequent reorientation and promote early mobilization
- Promote sleep at night
    - Seroquel 50 mg (providing QTc <500) and Melatonin 3 mg PO QHS
    - Control light and noise, decrease stimuli, clustering patient activities
- Perform RASS q4h or at any suspicion of withdrawal symptoms
- Pain-Analgesia-Delirium (PAD) alcohol withdrawal protocol

PAD alcohol withdrawal protocol for patients <u>not on ventilator</u>

If CIWA ≥8 or RASS >0, based on intensivist or advanced practice provider (APP) preference, will use one of the two options described below:

1. Benzodiazepine IV regimen:
    - Lorazepam 2 mg IV bolus q15min for CIWA 8-15 or RASS 1 or 2
    - Lorazepam 4 mg IV bolus q15min for CIWA 16-28 or RASS 3
    - Lorazepam 6 mg IV bolus q15min for CIWA >28 or RASS 4
    - Optional P.O. Diazepam 10 mg q6h with hold for RASS less than -1

If delirium symptoms persist despite Lorazepam IV regimen, per intensivist or APP preference, patient can be transitioned to Phenobarbital monotherapy option without loading bolus of Phenobarbital (see option 2 below) or add phenobarbital P.O. regimen to the Benzodiazepine IV regimen, as follows:

- Phenobarbital 97.2 mg PO q8h x6 doses
- Phenobarbital 64.8 mg PO q8h x6 doses
- Phenobarbital 32.4 mg PO q8h x6 doses

If delirium symptoms persist despite Lorazepam IV regimen and/or 20 mg/Kg/IBW of Phenobarbital:

- In addition to the above, initiate Dexmedetomidine as a third line therapy, at 0.4 mcg/kg/h to a maximum of 1.5 mcg/kg/h and adjust up/down as needed targeting RASS of 0.
- Use Haloperidol as a fourth line therapy 2.5 - 5 mg IV push every 10 - 30 min until RASS 0 or maximum dose of 30 mg providing QTc <500.
- Consider another diagnosis such as liver encephalopathy, CNS infection or trauma or endocrine abnormalities and treat accordingly if applicable.

2. Phenobarbital IV monotherapy regimen:

To be used in patients with definite diagnosis of alcohol withdrawal syndrome providing there are no contraindications*

- Give 10 mg/kg IBW of Phenobarbital IV infusion load over 30 min for CIWA ≥8 or RASS >0.
- Repeat Phenobarbital IV boluses q30 min PRN according to CIWA and RASS to a maximum cumulative dose of 20 to 30 mg/kg/IBW (20 mg/kg/IBW soft stop and 30 mg/kg/IBW hard stop).
  - CIWA 8-16 or RASS 1 - 2: Phenobarbital 130 mg IV slow push over 3 min
  - CIWA >16 or RASS ≥3: Phenobarbital 260 mg IV infusion over 15 min

- For patients with mild to moderate symptoms P.O. phenobarbital will be optional
  - 100 mg q60 min for CIWA 8-15 or RASS 1
  - 200 mg q60 min for CIWA ≥15 RASS ≥2

*Phenobarbital contraindications:

- Diagnosis of alcohol withdrawal is unclear. In this situation will use benzodiazepines based on RASS score
- Advanced cirrhosis with hepatic encephalopathy
- Acute intermittent porphyria
- Concurrent use of HIV medications
- Chronic use of phenobarbital as an antiepileptic agent

If delirium symptoms persist despite phenobarbital 20 to 30 mg/Kg/IBW:

- Do not give additional phenobarbital nor use benzodiazepines because they function synergistically and may produce respiratory depression.
- Initiate dexmedetomidine at 0.4 mcg/kg/h to a maximum of 1.5 mcg/kg/h targeting RASS of 0.
- Use Haloperidol 2.5 - 5 mg IV push every 10 - 30 min until RASS 0 or maximum dose of 30 mg providing QTc <500.
- Consider another diagnosis such as liver encephalopathy, CNS infection or trauma or endocrine abnormalities and treat accordingly if applicable.

Advantages of Phenobarbital compared to Benzodiazepines:

- Effect on both pathways implicated in the pathophysiology of alcohol withdrawal syndrome, the GABA and the AMPA-type glutamate receptors
- Does not induce paradoxical agitation/delirium
- When dosed appropriately in a patient with alcohol withdrawal, the risk of respiratory suppression or excessive somnolence are minimal

Dexmedetomidine caveats:

- Treat symptoms but does not address the underlying physiological problems (inadequate GABA signaling and excess NMDA activity).
- Does not have antiseizure effect. It should never be used as a sole agent for treatment of alcohol withdrawal syndrome.
- Advantages
  - It is titratable agent – may be adjusted up/down as needed.
  - Does not affect respiratory drive.
  - It has been shown to be beneficial for nocturnal delirium and promoting sleep at night.
  - It has both sedative and analgesic effects.

PAD alcohol withdrawal protocol for patients <u>on</u> ventilator

Propofol is the first-line sedative due to its effect on both GABA and glutamate - NMDA receptors.

- If RASS >0, initiate propofol IV infusion at 10 mcg/kg/h and titrate up to a maximum of 50 mcg/kg/min along with 50 mcg of fentanyl IV bolus q10min until patient is comfortable to a maximum of 200 mcg/h.
- If patient continues with RASS >0 despite above, initiate fentanyl IV infusion at 50 mcg/h and titrate up to a maximum of 200 mcg/h.
- If patient continues with RASS >0 despite above, initiate ketamine IV infusion, unless contraindicated, at 2 mcg/Kg/min to a maximum of 5 mcg/Kg/min.

If persistent RASS >0 despite propofol infusion at 50 mcg/kg/min, fentanyl IV infusion at 200 mcg/h and ketamine at 5 mcg/Kg/min, or at any time, the intensivist or APP based on his or her preference, will use either the benzodiazepine IV regimen or the phenobarbital IV monotherapy regimen as described above with the exception that the assessment of agitation will be based only on RASS rather than CIWA.

Appendixes

Richmond Agitation Sedation Scale (RASS)

Score	Term	Description
+4	Combative	Overtly combative, violent, immediate danger to staff
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive
+2	Agitated	Frequent non-purposeful movement, fights ventilator
+1	Restless	Anxious but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact to *voice* (> 10 seconds)
-2	Light sedation	Briefly awakens with eye contact to *voice* (< 10 seconds)
-3	Moderate sedation	Movement or eye opening to *voice* (but no eye contact)
-4	Deep sedation	No response to voice, but movement or eye opening to *physical* stimulation
-5	Unarousable	No response to *voice or physical* stimulation

Procedure for RASS Assessment

1. Observe patient
   a. Patient is alert, restless, or agitated. **(score 0 to +4)**
2. If not alert, state patient's name and *say* to open eyes and look at speaker.
   b. Patient awakens with sustained eye opening and eye contact. **(score –1)**
   c. Patient awakens with eye opening and eye contact, but not sustained. **(score –2)**
   d. Patient has any movement in response to voice but no eye contact. **(score –3)**
3. When no response to verbal stimulation, physically stimulate patient by
   e. shaking shoulder and/or rubbing sternum.
   f. Patient has any movement to physical stimulation. **(score –4)**
   g. Patient has no response to any stimulation. **(score –5)**

Alcohol Withdrawal Assessment Scoring Guidelines (CIWA - Ar)

Nausea/Vomiting - Rate on scale 0 - 7

0 - None
1 - Mild nausea with no vomiting
2
3
4 - Intermittent nausea
5
6
7 - Constant nausea and frequent dry heaves and vomiting

Tremors - have patient extend arms & spread fingers. Rate on scale 0 - 7.
0 - No tremor
1 - Not visible, but can be felt fingertip to fingertip
2
3
4 - Moderate, with patient's arms extended
5
6
7 - severe, even w/ arms not extended

Anxiety - Rate on scale 0 - 7
0 - no anxiety, patient at ease
1 - mildly anxious
2
3
4 - moderately anxious or guarded, so anxiety is inferred
5
6
7 - equivalent to acute panic states seen in severe delirium or acute schizophrenic reactions.

Agitation - Rate on scale 0 - 7
0 - normal activity
1 - somewhat normal activity
2
3
4 - moderately fidgety and restless
5
6
7 - paces back and forth, or constantly thrashes about

Paroxysmal Sweats - Rate on Scale 0 - 7.
0 - no sweats
1- barely perceptible sweating, palms moist
2
3
4 - beads of sweat obvious on forehead
5
6
7 - drenching sweats

Orientation and clouding of sensorium - Ask, "What day is this? Where are you? Who am I?" Rate scale 0 - 4
0 - Oriented
1 – cannot do serial additions or is uncertain about date

2 - disoriented to date by no more than 2 calendar days

3 - disoriented to date by more than 2 calendar days
4 - Disoriented to place and / or person

Tactile disturbances - Ask, "Have you experienced any itching, pins & needles sensation, burning or numbness, or a feeling of bugs crawling on or under your skin?"
0 - none
1 - very mild itching, pins & needles, burning, or numbness
2 - mild itching, pins & needles, burning, or numbness
3 - moderate itching, pins & needles, burning, or numbness
4 - moderate hallucinations
5 - severe hallucinations
6 - extremely severe hallucinations
7 - continuous hallucinations

Auditory Disturbances - Ask, "Are you more aware of sounds around you? Are they harsh? Do they startle you? Do you hear anything that disturbs you or that you know isn't there?"
0 - not present
1 - Very mild harshness or ability to startle
2 - mild harshness or ability to startle
3 - moderate harshness or ability to startle
4 - moderate hallucinations
5 - severe hallucinations
6 - extremely severe hallucinations
7 - continuous hallucinations

Visual disturbances - Ask, "Does the light appear to be too bright? Is its color different than normal? Does it hurt your eyes? Are you seeing anything that disturbs you or that you know isn't there?"
0 - not present
1 - very mild sensitivity
2 - mild sensitivity
3 - moderate sensitivity
4 - moderate hallucinations
5 - severe hallucinations
6 - extremely severe hallucinations
7 - continuous hallucinations

Headache - Ask, "Does your head feel different than usual? Does it feel like there is a band around your head?" Do not rate dizziness or lightheadedness.

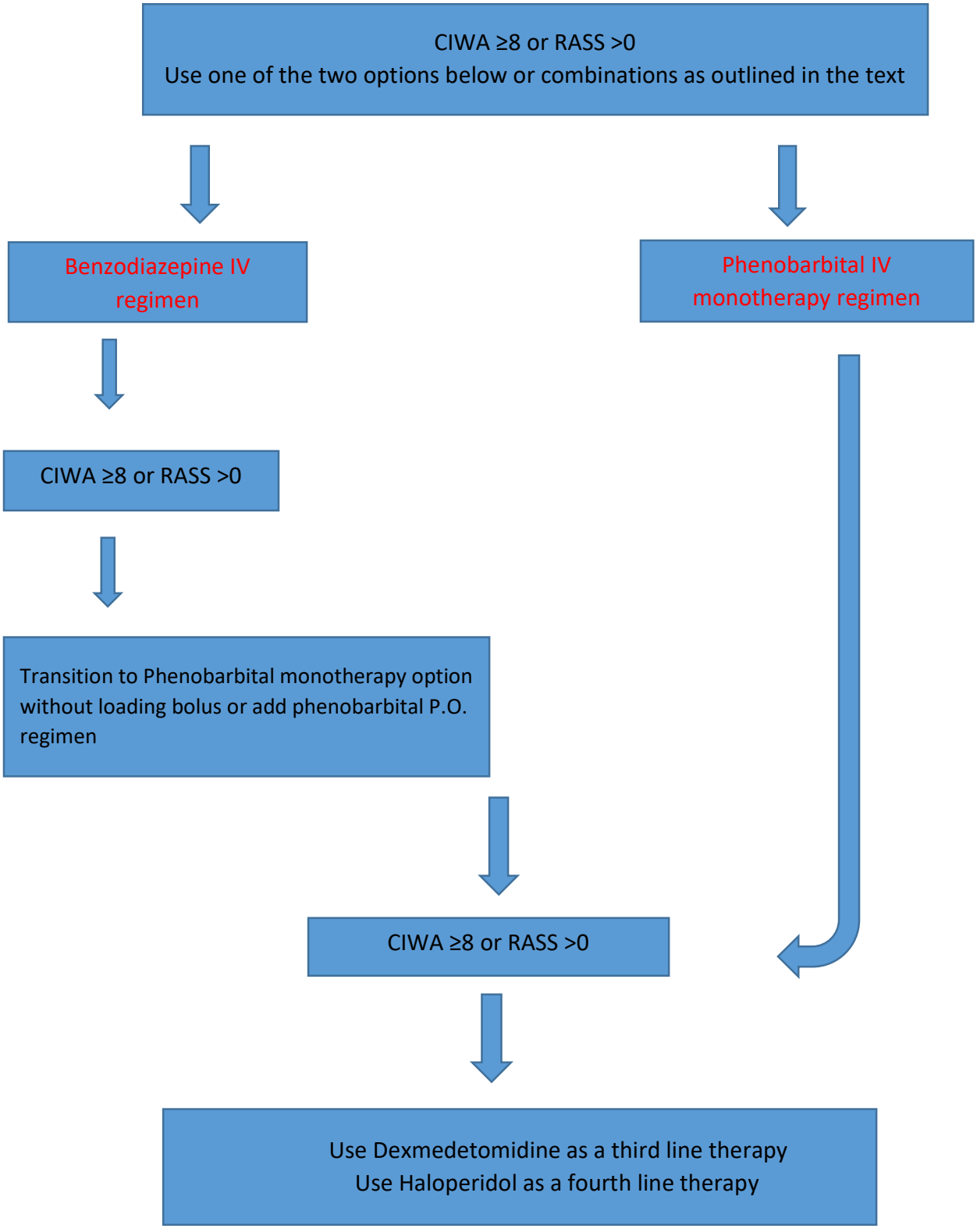
0 - not present
1 - very mild
2 - mild
3 - moderate
4 - moderately severe
5 - severe
6 - very severe
7 - extremely severe

Procedure:

1. Assess and rate each of the 10 criteria of the CIWA scale. Each criterion is rated on a scale from 0 to 7, except for "Orientation and clouding of sensorium" which is rated on scale 0 to 4. Add up the scores for all ten criteria. This is the total CIWA-Ar score for the patient at that time. Prophylactic medication should be started for any patient with a total CIWA-Ar score of 8 or greater (ie. start on withdrawal medication). If started on scheduled medication, additional PRN medication should be given for a total CIWA-Ar score of 15 or greater.
2. Document vitals and CIWA-Ar assessment on the Withdrawal Assessment Sheet. Document administration of PRN medications on the assessment sheet as well.
3. The CIWA-Ar scale is the most sensitive tool for assessment of the patient experiencing alcohol withdrawal. Nursing assessment is vitally important. Early intervention for CIWA-Ar score of 8 or greater provides the best means to prevent the progression of withdrawal.

Algorithm 1

Patients with severe alcohol withdrawal syndrome <u>not on ventilator</u>



Algorithm 2

Patients with severe alcohol withdrawal syndrome <u>requiring ventilator</u>

Following intubation, If RASS >0, initiate propofol IV infusion at 10mcg/kg/min and titrate up to a maximum of 50mcg/kg/min **PLUS** 50 mcg fentanyl IV bolus q10min to a maximum of 200 mcg until patient is comfortable. If needed, initiate, fentanyl infusion at 50 mcg/h and titrate up to maximum rate of 200 mcg/h.

RASS >0

Initiate ketamine IV infusion, unless contraindicated, at 2 mcg/Kg/min to a maximum of 5 mcg/Kg/min.

RASS >0

Use either the Benzodiazepine IV or the Phenobarbital monotherapy regimens or combinations as outlined in the text