

# Managing the Psychiatric Impact of a Health Crisis

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# Disclosures

“Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.”

## Psychiatric Manifestations of Acute COVID-19

- Delirium
- Psychosis
  - At least 42 cases reported thus far
  - Of patients with “altered mental status” in one series, nearly 25% had non-delirium psychosis
  - Several cases of brief reactive psychoses
  - One novel autoantibody detected
- Catatonia
- Depression and mania
- Exacerbation of serious mental illnesses

Varatharaj 2020; Watson 2021; McAlpine 2021

## Workup of COVID-19 Delirium

- Consider altered mental status as a prompt for COVID PCR testing in all patients
  - WHO now considered it a core symptom
  - 6<sup>th</sup> most common presenting sign and 37% don't have associated symptoms
- Basic bloodwork, including CRP, for COVID+ patients with delirium
- MRI may reveal specific pathology (silent CVA's, encephalitis, AHNE)
- EEG and CSF findings less likely to be helpful
- Utility of test must be balanced with risks of further exposure

Kennedy 2021

## How Do We Approach Management of Delirium in COVID-19?

- As with all delirium, medications manage sequelae rather than treating the delirium
- Consider using medications for agitation (hyperactive delirium), for prominent perceptual disturbances, or for signs of catatonia/akinetic mutism
- Increased concern for EPS given reports of increased tone and signs of akinetic mutism
- Increased concerns for QT prolongation given use of hydroxychloroquine, azithromycin and other agents
- Parenteral agents preferred given severity of agitation and medical co-morbidities

# Management of COVID-19 Delirium

Step 1	
<b>Melatonin</b>	Start melatonin at 1-3mg daily at 1800 hours. Dose regularly at the same time. Exercise caution in patients for whom there is evidence of inadequate immune response.
Step 2	
<b>Alpha-2 Agonist</b>	Consider using dexmedetomidine for ICU patients. Wean by no more than 20% per day. Can cross taper with clonidine patch, starting 0.1mg patch the night before wean attempt. Oral clonidine 0.1-0.3mg three times per day can also be used for agitation.
Step 3	
<b>Antipsychotic Agent</b>	Consider antipsychotic agent for ongoing agitation. Low-potency agents preferred. May consider aripiprazole specifically for hypoactive delirium with perceptual disturbance. Use caution with antipsychotics if evidence of EPS, akinetic mutism or catatonia.
Step 4	
<b>Valproic Acid or Trazodone</b>	If additional agents required, or if antipsychotic agents are relatively contraindicated, consider using valproic acid 15mg/kg per day in 3 divided doses PO or IV daily or trazodone 12.5-50mg every 6 hours as needed. Titrate to effect.
Step 5	
<b>Dopamine Agonist</b>	If evidence of akinetic mutism or catatonia, consider adding amantadine 100mg daily (titrated over 3-4 days to 600mg daily) or methylphenidate 5-10mg twice daily. Monitor for seizures with amantadine and worsening

# Antidepressants

- RCT found patients given fluvoxamine 100mg daily x 15 days during mild illness, had a lower likelihood of clinical deterioration compared with those given placebo
  - 152 patients
  - Clinical deterioration occurred in 0 in the fluvoxamine group and 6 in the placebo group
- Observational study found association between receiving antidepressant within 48 hrs of admission and reduced risk of intubation or death in hospitalized patients
  - Held for SSRI and non-SSRI antidepressants
  - Particularly significant for fluoxetine, escitalopram, paroxetine, venlafaxine
- Prior studies suggest several antidepressants may inhibit sphingomyelinase activity, which may prevent infection of epithelial cells with SARS-CoV-2
- Antidepressants may also prevent cytokine storm (Sigma-1 inhibition) and reduce inflammatory mediators
- Fluoxetine may have antiviral effects on SARS-CoV-2

Hoertel 2021; Lenze 2020; Zimniak 2020; Carpinteiro 2020

# SMI Patients with COVID-19

- Schizophrenia-spectrum illnesses are one of the strongest risk factors for mortality in COVID
  - [OR], 2.67; 95%CI,1.48-4.80
- Clozapine
  - Treatment with clozapine associated with increased risk of COVID-19
  - Lymphopenia common
  - Higher rates of pneumonia in patients on clozapine
  - Clozapine levels may increase by 2-fold (consider cutting dose in half for any patients who develop fever)

Dotson 2020, Bilbul 2020



# Suicidality

- Suicide rates were increased in the setting of SARS, particularly in those over 65 years
- Suicide rates in MA did not increase during the stay-at-home advisory
- Google searches for suicide decreased during early pandemic
- Case reports and series emerging of suicidality during COVID-19
  - Common include concern about infecting family members, social pressure and xenophobia in the setting of upper respiratory symptoms, fear of isolation, unreliable information sources (e.g. social media, word of mouth), inability to safely manage quarantine, and a lack of access to resources (including food, medicines, or health supports)
  - 23/50 cases of suicidality on the MGH Consultation Service between March and May 2020 were directly related to COVID-19

Halford 2020

# Post-COVID Outcomes

- Prior history of psychiatric illness is an independent predictor of mortality
- 55% of COVID-19 survivors had symptoms of depression, anxiety or PTSD
- Being female and having a prior psychiatric history were independent risk factors
- Inflammation was positively associated with symptoms of depression and anxiety
- In another study, perceived discrimination was the biggest risk factor of psychiatric complications

Li 2020, Mazza 2020

# Post-COVID Outcomes

- Risk of first psychiatric diagnosis following COVID was 2x that of risk of first psychiatric illness after flu
- 18.1% of patients developed psychiatric diagnosis in 14-90 days (6% first diagnosis)
- 1.6% developed first diagnosis of dementia

Taquet 2020

## Cognitive Outcomes in Hospitalized Patients

- Study of 57 hospitalized patients
- 84% previously living independently
- 88% of study patients had hypoxemic respiratory failure and 77% required intubation
- Deficits in working memory, set-shifting, divided attention and processing speed
- Executive dysfunction not associated with intubation length or premorbid disease

# Long COVID

- Emerging evidence of lingering fatigue and subjective cognitive dysfunction in some patients with COVID
- Often mild initial infection (not hospitalized)
- Chronic (>4-12 weeks) disabling symptoms
- Clinical picture resembles Myalgic Encephalomyelitis (CFS)
- FDG PET reveals hypometabolism in cerebellum, pons/medulla, thalamus, amygdala and hippocampus
- Some objective evidence of cognitive dysfunction emerging
- Current recommendation is for PT, OT, Speech Therapy
- Medications thus far not shown to have impact
- Implications for return to work, disability, etc