Canadian Consortium for Early Intervention in Psychosis

Medication Management in the Virtual Care Environment

August 12, 2020

Welcome from the CCEIP

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President of the CCEIP
Nova Scotia Early Psychosis Program

The Canadian Consortium for Early Intervention in Psychosis (CCEIP) is a national, not-for-profit organization of clinicians and researchers dedicated to improving the quality of care for individuals in early phase psychosis.

MISSION: To enhance optimum care for Canadians in the early phase of psychosis through improved service models and the generation and translation of knowledge.

Social

- Website
  - For doctors and healthcare practitioners: http://epicanada.org/
  - For patients and their family: https://www.earlypsychosisintervention.ca/
- Social Media
  - Twitter: @EPI_Canada

Learning Series

The CCEIP saw an opportunity to bring together the early psychosis clinical community in virtual meetings to present new information and challenge clinical decisions in best interest of patient care. To do this we offered a series of 4 learning events which focused on clinical considerations aligned to best practices in our new virtual care environment.

- Past topics: PLEASE SEE OUR WEBSITE/RESOURCES
  - Schizophrenia and COVID-19.
  - Maximizing The Virtual Appointment Experience For You And Individuals With Early Phase Psychosis.
- Subsequent topics:
  - Virtual Delivery of Multidisciplinary Team-Based Care: August 19th from 12:00 – 12:45 pm.

Today's Objectives

After attending this Webinar, you will be better able to:

- Monitor antipsychotic medications in the virtual care environment, including dose adjustments, switching, side effect management and blood monitoring.
- Optimize outcomes through the appropriate use of antipsychotic medication, tailored to the patient.

Agenda

• 12:00 – 12:10	Housekeeping, Welcome and Introductions
• 12:10 – 12:35	Medication Management in the Virtual Care Environment
• 12:35 – 12:45	Q&A

Today's Speaker

Pierre Chue, MBBCh, FRCPsych, LMCC, FRCPC, DABPN, MSc, CCST.
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Disclosure

Potential for conflict(s) of interest:

- Dr. Chue has received funding from organizations whose product(s) may/are being discussed in this presentation: Sunovion, Astra Zeneca, Bristol Myers Squibb, Otsuka, Eli Lilly, Glaxo Smith Kline, Janssen, HLS, Mylan, Lundbeck, Novartis, Pfizer, Hoffmann La Roche, Sunovion, Paladin, Valeant, Allergan, Alkermes, AbbVie.

Mitigating potential bias:

- Clinical trial data, peer reviewed publications, approved communications from FDA including US Package Inserts (USPI), Health Canada including Product Monographs (PM), and European Medicines Agency (EMA) summary of product characteristics (SmPC).

Disclaimer

- This slide presentation may include evolving scientific information that has not been reviewed and approved by Health Canada.
- This information is intended for your educational purposes and to provide pertinent data to assist you in forming your own conclusion(s). Providing this information does not constitute any recommendation for use.
- The use of pharmaceutical products should always be in accordance with the approved indications that are described in the relevant Product Monographs.

Introduction

- Currently almost 10 million individuals have been affected by COVID-19 worldwide resulting in an unprecedented and significant impact on the general population and particularly on those suffering from mental illness.
- The stress-diathesis model of psychiatric disorders is further impacted by the enormous psychosocial changes, transformations in health care delivery and the direct physiological effects of COVID-19.
- Healthcare professionals have had to rapidly adjust practice to develop practical solutions to mitigate the psychiatric risks associated with COVID-19.

Thomas RK, et al. JPN 2020;45(4):229-233

Introduction (cont'd)

- The lack of guidance on how psychiatric services need to adapt to COVID-19 has lead to inconsistent reactions with potential negative consequences on patient health outcomes.
- The increase in novel and creative interventions including virtual consultation has reflected the changes in access to hospital and clinic-based services.
- However, for psychiatric patients the difficulties in accessing specific interventions that still require direct contact such as ECT, LAIs or required blood monitoring has proved challenging.

Thomas RK, et al. JPN 2020;45(4):229-233

Neurological and neuropsychiatric complications of COVID-19

- COVID-19 exhibits neurotropic properties & crosses the Blood-Brain Barrier (BBB).
- Neurological & neuropsychiatric sequelae of COVID-19 are common and occur in younger patients:
  - Cerebrovascular events (ischemic stroke, intracerebral haemorrhage, CNS vasculitis).
  - Altered mental status (encephalopathy, encephalitis, new-onset psychosis, neurocognitive syndromes, affective disorders).
- Symptoms identified in a systematic review & metanalysis (n=3559) included:
  - Acute illness – confusion, depressed mood, anxiety, impaired memory, & insomnia.
  - Post-illness - depressed mood, insomnia, anxiety, irritability, memory impairment, traumatic memories, & sleep disorder.

Varatharaj A et al. Lancet Psychiatry June 25 2020; Rogers JP, et al. Lancet Psychiatry 2020; 7: 611–27; Wu Y, et al. Brain, Behavior, & Immunity 2020; 87:18–2219

COVID-19 Challenges in Providing Care to Psychiatric Patients

- Healthcare teams must increase vigilance, aiming at reducing the risk of patient contamination and community spread.
- What are the factors to consider?
  - Patient's functional status – ability to comply with current Public Health requirements.
  - Patient's ability to realize and express that they are not well in the event of infection.
  - Potential impact on other residents of the patient's living environment, & impact that their living environment may have on them.
  - Potential impact of the means of transportation to get to clinics/labs.
  - Contamination rate in a given region.
  - Capacity of the local mental health care system to provide sufficiently close follow-up.

1. Recommendations from the provincial ad hoc committee made up of Drs Pierre Chue, Patrick White, Jan Banash, Tim Ayas, Toba Oluboka, David Tano, Allison Mitchell, Izu Nwachuckwu and Ron Pohar inspired by international expert consensus (April 2020)

Are Psychiatric Patients at Greater Risk During COVID-19?

- Psychiatric patients may have limited:
  - Understanding/awareness of infection.
  - Ability to follow social distancing/restrictions.
- Increased accrued health risks:
  - Disease factors:
    - Immune status.
  - Physical comorbidities:
    - Diabetes.
    - CVS disease.
  - Lifestyle factors:
    - Smoking.
    - Sedentary.
    - Environment e.g., group home/homeless.

Sedentary status + stress + smoking = ↑ risk of cardiovascular morbidity

- Medication factors:
  - Increased medication adverse effects (AEs) & Drug-Drug Interactions (DDIs) due to COVID-19's effects on organ systems.

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COVID-19 & Antidepressants

- COVID-19 associated coagulation abnormalities & many COVID-19 patients are receiving anticoagulant therapy:
  - SSRIs and SNRIs are associated with impaired platelet aggregation & abnormal bleeding.
- COVID-19 associated tachyarrhythmias and cardiac injury & COVID-19 medications can cause QT prolongation:
  - S-citalopram and TCA can cause QT prolongation.
- COVID-19 associated acute liver injury:
  - Duloxetine can be associated with drug-induced liver injury.
- COVID-19 associated with seizures:
  - Bupropion can lower seizure threshold.

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COVID-19 & Benzodiazepines

- COVID-19 associated delirium is prevalent & severe:
  - Benzodiazepines can exacerbate delirium and cognitive problems.
- COVID-19 is associated with prominent respiratory symptoms;
  - Benzodiazepines can suppress respiratory drive
- COVID-19 treatment Drug-drug Interactions (DDIs):
  - Lopinavir/Ritonavir are contraindicated with midazolam & triazolam (& can raise levels of some other benzodiazepines) through CYP450 inhibition

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COVID-19 & Mood Stabilizers

- Lithium
  - COVID-19 associated potential for acute kidney injury:
    - Risk of lithium toxicity due to decreased clearance.
    - High lithium levels are nephrotoxic.
- Carbamazepine
  - COVID-19 associated with leukopenia and lymphopenia:
    - Carbamazepine associated with leukopenia & aplastic anemia.
  - COVID-19 associated acute liver injury:
    - Carbamazepine with potential for drug-induced liver injury.

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COVID-19 & Mood Stabilizers

- Sodium valproate
  - COVID-19 associated coagulation abnormalities (PT and aPTT prolongation, thrombocytopenia):
    - Valproate is associated with thrombocytopenia.
  - COVID-19 associated acute liver injury:
    - Valproate is associated with potential for drug-induced liver injury.
- Topiramate & pregabalin
  - COVID-19 associated potential for acute kidney injury:
    - Increased adverse effects e.g., paraesthesia with topiramate & sedation with pregabalin due to decreased clearance.

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COVID-19 & Antipsychotics

- COVID-19 associated leukopenia and lymphopenia:
  - Risk of aplastic anemia or lymphopenia, especially with phenothiazines.
- COVID-19 associated coagulation abnormalities (PT and aPTT prolongation, thrombocytopenia):
  - Risk of thrombocytopenia e.g., chlorpromazine.
- COVID-19 associated tachyarrhythmias, cardiac injury & DDIs:
  - Risk of QTc prolongation e.g., ziprasidone.
- COVID-19 associated acute liver injury:
  - Risk of drug-induced liver injury e.g. chlorpromazine, olanzapine.
- COVID-19 associated seizures:
  - All antipsychotics affect seizure threshold.

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COVID-19 & Clozapine

- COVID-19 associated with leukopenia and lymphopenia:
  - Clozapine associated with neutropenia & agranulocytosis (rarely lymphopenia or aplastic anemia).
- Clozapine is associated with risk of myocarditis:
  - It is unknown if the risk of myocarditis is increased during a COVID-19 infection.
- Blood monitoring is mandatory for all patients receiving clozapine:
  - Difficulty in completing blood monitoring – social distancing, fear, access.
  - Frequency of blood monitoring – Health Canada requirements.
  - Point-of-care (POC) monitoring – PRONTO.

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Hematologic Monitoring

- **Health Canada** has recently offered in collaboration with the different Clozapine Assistance Networks a degree of **flexibility** in **clozapine blood monitoring** during this period **(this does not mean no blood monitoring).**
- **Risk and benefits** associated with any treatment and its modifications **must be weighed for each individual patient** and **discussed** with the patient or their substitute decision maker during the **informed consent process**.
- Consider the following factors when deciding whether or not to extend the frequency of blood work:
  - Prevalence of COVID-19 in the community.
  - Most recent recommendations from public health authorities.
  - Patient length of time on clozapine.

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Hematologic Monitoring (cont'd)

- During periods of **less frequent** hematological monitoring, **increased vigilance** will be required to promptly identify patients on clozapine who have a **fever, chills** or have **other symptoms** suggestive of **infection**:
  - **Sore throat.**
  - **Flu-like symptoms.**
  - **Cough.**
  - **Lethargy.**
  - **Stiffness / Muscle pain.**
  - **Mucosal ulceration.**
  - **Loss of taste and smell.**
  - **Difficulty breathing.**

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Hematologic Monitoring (cont'd)

- Regardless of hematologic monitoring schedule, regular clinical assessments should be conducted, including:
  - Assess patients' mental status.
  - Confirm that they show no signs of infection.
  - Monitor adverse reactions/events to medications.
- These follow-ups could be carried out in person, by telephone, or by telehealth consultations (in accordance with the recommendations, policies, and procedures of various professional bodies and institution policies.
- Medical orders to change the frequency of hematological monitoring should specify that this is a temporary measure in the context of the current COVID-19 pandemic.
- The dispensing pharmacy and clozapine registry involved in these patients' care should be promptly notified.

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COVID-19 & Clozapine

- COVID-19 associated with seizures:
  - Clozapine can lower seizure threshold; 5% risk with 500 mg dose.
- Clozapine is associated with increased risk of pneumonia and its complications.
- Clozapine levels **increase** with acute infection through cytokine mechanism resulting in increased adverse effects e.g., sedation, seizures.

Bilbul M, et al. Psychosomatics 2020 May 18

COVID- 19 & Long-acting injections (LAIs)

- The use of LAIs addresses covert non-adherence and partial adherence & is associated with decreased relapse and reduced mortality.
- However, LAIs remain underutilized because of stigma, lack of infrastructure and poor access.
- Further, some COVID-19 recommendations have included avoiding LAIs, switching to oral antipsychotics or extending intervals between injections.

Ifteni P, et al. Schizophr Res2020 Jun; 220: 265–266; www.psychiatry.org/File%20Library/Psychiatrists/APA-Guidance-Long-Acting-Injectables-COVID-19.pdf; https://saskpharm.ca/document/5947/COVID-19_Pharmacist_Injections_04232020.pdf; www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Coronavirus/Managing%20Depots%20and%20LAIs%20During%20COVID-19%20-%20CMHP%20and%20RPS%20Endorsed.pdf?ver=2020-05-01-163514-263; www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/managing-depots-during-covid.pdf?sfvrsn=fdaffc8b_2

Risks of Switching to Oral Antipsychotics

- Relapse or destabilization, should the dose of oral medication be too low or if the patient has reduced adherence to the oral medicine.
- Exacerbation of condition due to stress and anxiety from the switch.
- Potential medication errors during the cross over.
- Difficulties in working out equivalent doses requiring periods of dose adjustments and more frequent contact.
- Combined adverse drug reactions (ADRs)during the period of crossover or ADRs due to the oral dose equivalent being too high.

lwww.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/managing-depots-during-covid.pdf?sfvrsn=fdaffc8b_2

COVID-19 & Long-acting injections (LAIs) (cont'd)

- COVID-related changes in LAI utilization patterns depend on jurisdiction, policy & COVID prevalence in the community.
- Romania: LAI use in hospital clinic decreased by 49% for risperidone LAI & 90% for olanzapine LAI.
- USA (Pittsburg): 10% reduction in LAI use.
- Alberta: Increase in switches to LAIs & use of 3/12 LAIs.

Ifteni P, et al. Schizophr Res2020 Jun; 220: 265–266; Gannon JM, et al. Schiz Res 2020; Chue P. Personal Communication 2020

Use of Long-acting Injectables as a Clinically Necessary Treatment

During this COVID-19 pandemic the APA encourages hospitals and other facilities to include the ongoing use of long-acting injectables (LAI) for patients with high-risk chronic illness as a necessary procedure.

COVID-19 Pandemic Guidance Document

Prepared by the APA Committee on the Psychiatric Dimensions of Disaster and COVID-19

www.psychiatry.org/File%20Library/Psychiatrists/APA-Guidance-Long-Acting-Injectables-COVID-19.pdf;

Summary

- The complications of COVID-19 &treatments impact on many organ systems & contribute to potential drug-drug interactions.
- COVID-19 crosses the BBB resulting in neurologic & neuropsychiatric effects which further complicates the management of psychiatric disorders.

Summary (cont'd)

- Quality evidence-based psychiatric care remains essential and must continue to be available for all patients:
  - This should include clozapine & LAI initiation.
- Health care professionals need to be cognizant of the unique challenges faced by psychiatric patients.
- Psychotropic medications have their own potential for drug-interactions and end-organ adverse effects.