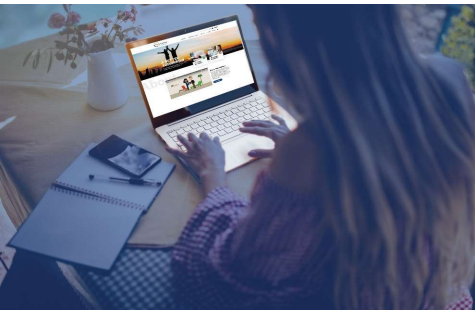


WELCOME

Clozapine & LAI Virtual Forum

March 1, 2023 | 4:00 – 4:45 pm ET

The Clozapine & LAI Virtual Forum is a peer-to-peer, interactive dialogue between psychiatrists, nurse practitioners, and other prescribing clinicians. It is informal, no registration required — just join our Zoom call and share your challenges and questions on the month's trending topic around either clozapine or LAIs.



TODAY'S TOPIC:
Managing Sedation Due to Clozapine



MODERATORS

Robert Cotes, MD

SMI Adviser Physician Expert; Emory University

Dr. Robert Cotes, MD, is an Associate Professor at Emory University School of Medicine in the Department of Psychiatry and Behavioral Sciences. He has interest in clozapine, characterizing persistent symptoms of schizophrenia, understanding cardiometabolic side effects of antipsychotic medications, and first episode psychosis. Disclosures: Otsuka, Roche, Alkermes (Research Funding), Saladax Biomedical (Consultant), and Clinical Care Options (Speaker)

Donna Rolin, PhD, APRN

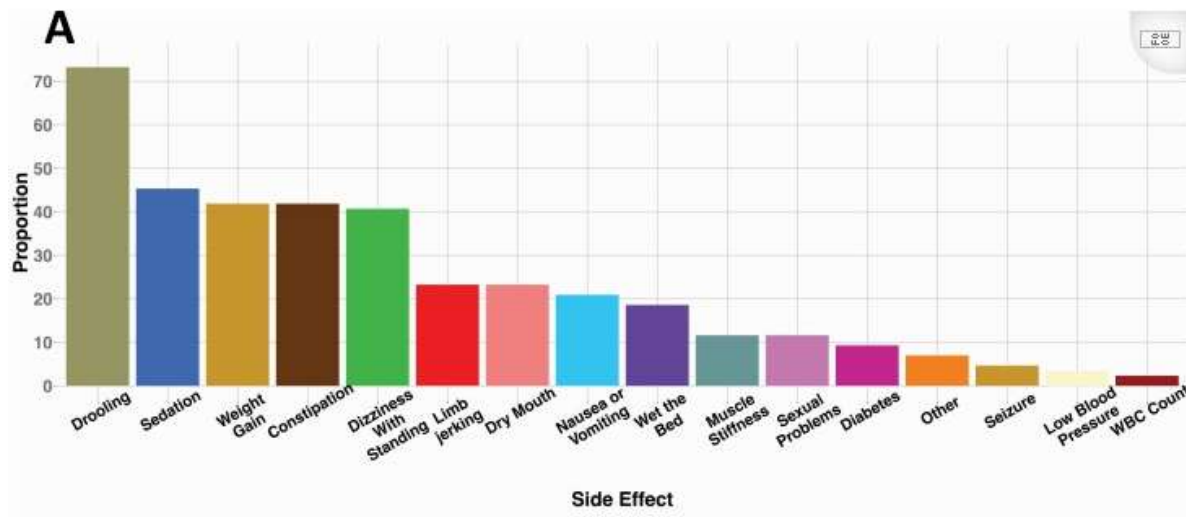
SMI Adviser Nursing Expert; University of Texas, Austin

Dr. Donna Rolin is Clinical Associate Professor and the Director of the Psychiatric Mental Health Nurse Practitioner program at the University of Texas with 23 years of experience in psychiatric nursing, including inpatient, community, forensic, and older adult settings.

Discussion Questions for Virtual Forum: Questions

- How big of a problem is sedation due to clozapine for your patients? Do you see this frequently?
 - How do you ask patients about this?
- Have you ever had anyone discontinue clozapine due to sedation?
- How do you typically manage clozapine-induced sedation?
 - What non-pharmacologic strategies do you use?
 - Do you use pharmacologic strategies?

Patient Reported Frequency of Sedation for Clozapine



- InterSePT
 - Drowsiness/sedation: 39%
 - Dizziness/Vertigo: 19%
 - Headache: 7%
 - Tremor: 7%
- CATIE Phase II
 - Sedation: 45%

Sharma, S., Kopelovich, S. L., Janjua, A. U., Pritchett, C., Broussard, B., Dhir, M., . . . Cotes, R. O. (2021). Cluster Analysis of Clozapine Consumer Perspectives and Comparison to Consumers on Other Antipsychotics. *Schizophr Bull Open*, 2(1), sgab043; Meltzer, H. Y., Alphas, L., Green, A. I., Altamura, A. C., Anand, R., Bertoldi, A., . . . Potkin, S. (2003). Clozapine treatment for suicidality in schizophrenia: International Suicide Prevention Trial (InterSePT). *Arch Gen Psychiatry*, 60(1), 82-91. doi:10.1001/archpsyc.60.1.82; McEvoy, J. P., Lieberman, J. A., Stroup, T. S., Davis, S. M., Meltzer, H. Y., Rosenheck, R. A., . . . Investigators, C. (2006). Effectiveness of clozapine versus olanzapine, quetiapine, and risperidone in patients with chronic schizophrenia who did not respond to prior atypical antipsychotic treatment. *Am J Psychiatry*, 163(4), 600-610. doi:10.1176/appi.ajp.163.4.600

Key Facts on Sedation Due to Clozapine

Related to
muscarinic and H₁
antagonism

Likely associated
with higher levels

Appears early and
may improve with
time

Common reason
for early
discontinuation

Sometimes not
noticed until
someone is more
stable

Legge, S. E., Hamshere, M., Hayes, R. D., Downs, J., O'Donovan, M. C., Owen, M. J., . . . MacCabe, J. H. (2016). Reasons for discontinuing clozapine: A cohort study of patients commencing treatment. *Schizophr Res*, *174*(1-3), 113-119. doi:10.1016/j.schres.2016.05.002

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Considerations for Clozapine Titrations

Prior to starting clozapine: Minimize exposure to benzodiazepines and anticholinergics, Encourage patient to start monitoring sedation and report if issues occur

Consider only bedtime, rather than divided dosing

Individualize titration based on clinical scenario, demographics, other medications, and clinical response

Carefully cross-taper other sedating antipsychotics with clozapine

Revert to the prior clozapine dose, if possible, if the patient experiences significant sedation. After 3-7 days, may resume titration. Consider checking a level.

Meyer JM, Stahl SM (2019). [The Clozapine Handbook: Stahl's Handbooks, Cambridge University Press.](#)

STOP-Bang Questionnaire for Obstructive Sleep Apnea

STOP		
Do you SNORE loudly (louder than talking or loud enough to be heard through closed doors)	Yes	No
Do you often feel TIRED , fatigued, or sleepy during daytime?	Yes	No
Has anyone OBSERVED you stop breathing during your sleep?	Yes	No
Do you have or you being treated for high blood PRESSURE ?	Yes	No
BANG		
BMI more than 35kg/m ²	Yes	No
AGE over 50 years old	Yes	No
NECK circumference > 16 inches	Yes	No
GENDER (biologic sex): Male?	Yes	No

Low Risk: Yes to 0-2 questions

Intermediate Risk: Yes to 3-4 questions

High Risk: Yes to 5-8 questions

Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. *Chest*. 2016 Mar;149(3):631-8. doi: 10.1378/chest.15-0903. Epub 2016 Jan 12. PMID: 26378880.

Pharmacologic Interventions

- Barcelona prospective cohort on clozapine
 - Dose reduction = 4/22 (18.2%) reduced number of hours slept
 - Average dose reduction 44 mg
 - Aripiprazole augmentation = 4/23 (17.4%) reduced number of hours slept
 - Average aripiprazole 7 mg

Ramos Perdigués, S., Sauras Quecuti, R., Mané, A., Mann, L., Mundell, C., & Fernandez-Egea, E. (2016). An observational study of clozapine induced sedation and its pharmacological management. *Eur Neuropsychopharmacol*, 26(1), 156-161. doi:10.1016/j.euroneuro.2015.11.006

Pharmacologic Interventions

- Modafinil

- Freudenreich et al. 2009

- Double-blind, placebo-controlled pilot study
 - Dose range 200-300 mg
 - No benefit, no worsening

- Symptomatic worsening in case reports (Ozer and Demir, 2010)

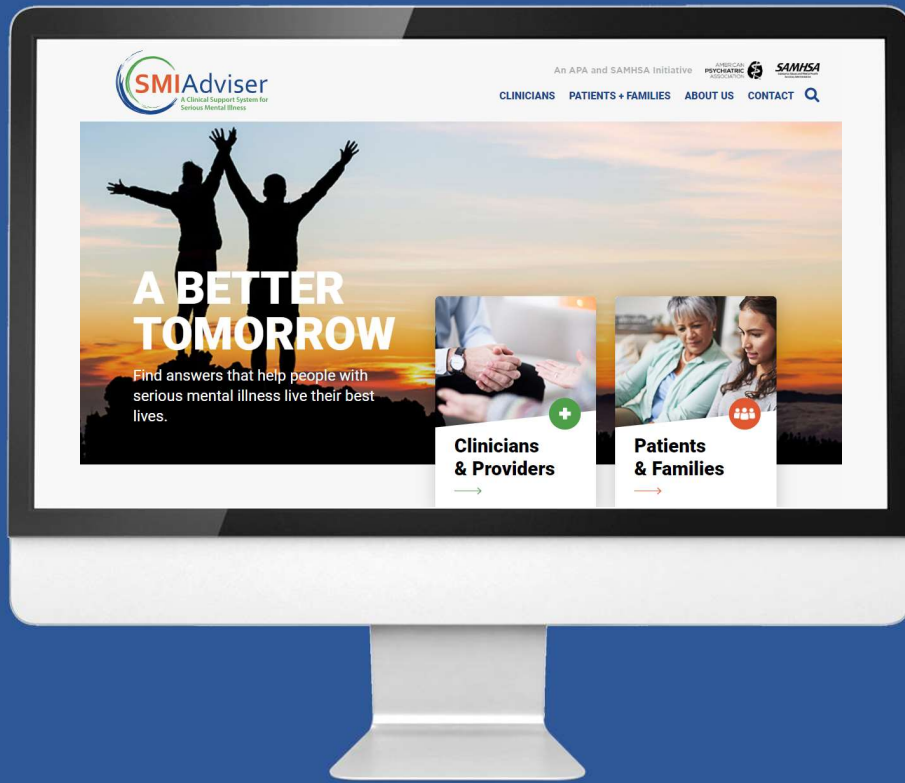
- Methylphenidate

- Only case report/case series level data (Burke and Sebastian, 1993; Skoretz and Tang, 2016)

Freudenreich, O., Henderson, D. C., Macklin, E. A., Evins, A. E., Fan, X., Cather, C., . . . Goff, D. C. (2009). Modafinil for clozapine-treated schizophrenia patients: a double-blind, placebo-controlled pilot trial. *J Clin Psychiatry, 70*(12), 1674-1680. doi:10.4088/JCP.08m04683

FEEDBACK

Please help us improve the Clozapine & LAI Virtual Forum by completing this survey:
<http://smiadviser.org/forumfeedback>



Pre-submit Cases

www.smiadviser.org/vfcases

UPCOMING VIRTUAL FORUM

Physical Health and Cardiometabolic Monitoring for Patients on LAIs

April 5, 2023 @4-4:45pm ET

For additional questions and resources – join the Clozapine and LAI Centers of Excellence Exchange Community

- www.smiadviser.org/cloz_lai_signup

An APA and SAMHSA Initiative

