Tobacco Treatment in People with Schizophrenia

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Learning Objectives:

- Develop an evidence-based approach to assessment and treatment for tobacco use disorder in people with schizophrenia and other serious mental illness.

- Understand an approach to developing a tobacco-free mental health and addictions facility for the benefit of patients, staff and visitors.
Medical Impact of Tobacco

- Tobacco use is the leading cause of preventable death in Western world (Giovino, GA, 2007)

- Over 470,000 deaths per year in USA and >50,000 annual deaths in Canada attributable to tobacco addiction (George, TP, 2015. Chapter 32, Cecil Textbook of Medicine, 25th Edition)

- Significant contributor to cardiovascular, pulmonary disease and to many cancers (e.g. lung, throat) (George, 2015)

- Reducing smoking leads to some health improvements (e.g. better breathing and exercise tolerance), but reductions in cardiac, pulmonary and oncological disease are only seen when quitting smoking (George, 2015)
Mental Health Impact of Tobacco

- Higher rates of smoking in mentally ill (MI) populations makes them more vulnerable to tobacco-related medical illness (Mackowick et al., 2012)

- People with MI spend up to 25% of their disability income on tobacco (Ziedonis et al., 2008)

- Tobacco addiction shortens the lives of people with MI by 12-13 years (Williams et al., 2011)

- Rates of quitting smoking for MI smokers are 1/3 to 1/2 rates in the general population (Morisano et al., 2009)

- Quitting smoking in MI populations leads to better psychiatric and substance use disorder outcomes, including reductions in depression and alcohol use, and less suicidal behaviours and aggression (Mackowick et al., 2012; Morozova et al., 2015)
Prevalence of Tobacco Smoking in Clinical Samples of People with Mental Illness and Addictive Disorders

Current Smoking among Adults Aged 18 or Older

Based on Serious Psychological Distress Status of Previous Month (NHIS, 1997 to 2011)

*Difference between estimate and estimate for 2011 is strategically significant at the 0.5 level*
Tobacco Bans in Hospital Settings

Advantages

- Great opportunity to provide motivational interventions for those not initially willing to try to quit (a “teachable moment”)

- Reduction in episodes of seclusion and restraint, decreased PRN* use and Length Of Stay (LOS)

- The goals of a smoke-free work environment are promoted and are consistent with wellness interventions that are being implemented in most inpatient settings

Disadvantages

- Inpatients generally not interested in quitting, as this is low on their “hierarchy of needs”

- Staff are often reluctant as it can be perceived as a distraction to treatment plans, and is a critical “positive” reinforcer

- Lack of training of unit staff or other qualified people to conduct smoking cessation counseling

- Unmotivated inpatients pose a barrier to success of those few patients wanting to quit

*Lawn and Pols, 2005; Moss et al., 2010
*Moss et al., Am. J. Addict. 2010

*PRN – Known as medications that are taken “as needed”
Key Elements of Tobacco Free CAMH

1. No Smoking (or Vaping) at any campus site (2 main campuses + outpatient satellites)

2. No Possession of Tobacco Products on the Premises

3. Presence of Community “Ambassadors”, Patients and Staff who promote tobacco-free CAMH though a Wellness and Recovery Culture using a positive reinforcement approach and act as “Champions” for the Initiative
Staff and Patient Attitudinal Survey Results

10 %
- Increase in staff confidence in having appropriate access to team / management support or training required to comply with the tobacco-free policy (12% to 22%)

7 %
- Increase in awareness of how to help / where to refer a client if they want to quit (13% to 20%)

19 %
- Increase in the support of the creation of a tobacco-free policy at CAMH (48% to 67%)

17 %
- Increase in the belief that lowering tobacco use on CAMH property is important (51% to 68%)

16 %
- Increase in contributing to the success of the policy by not smoking at CAMH (56% to 72%)

Riad-Allen et al., 2016. Am. J. Addict., in press
Effects of CAMH Tobacco Free on Aggression (Code Whites)

An approach to tobacco cessation in smokers with schizophrenia
Quitting smoking is easy –
I’ve done it several hundred times ...

- Mark Twain
Case #1

- 40 year old black male with schizophrenia, never married, lives in a shelter in a major city.

- Smokes 3 packs per day (illegal cigarettes), first cigarette is within 2 minutes of awakening. He also started smoking e-cigarettes (“Vapes”).

- Multiple quit attempt failures since started smoking at age 14. Has tried all NRTs (gum, patch, inhaler)

- Psychosis is well-managed with depot antipsychotic (Risperidone Consta), at 50 mg qmonth. Takes some oral risperidone for breakthru symptoms

- Family Hx+ for CAD, Lung CA. He himself had anterior wall MI 6 months ago, after months of chest pain, took himself to local general hospital.

- He doesn’t really want to quit, but does not want to die from (another) MI …
Question

- What can we do for this man?
Vulnerability markers for tobacco addiction in schizophrenia

Reduced Smoking – A Viable Target or Not?

- Many smokers are simply unable to quit smoking.

- Should sustained reductions in smoking been considered a goal of tobacco treatment or should reduction be a transitional goal towards eventual smoking abstinence (Hughes, 2002; George and Vessicchio, 2002; McChargue et al., 2002)?

- A recent study suggests that sustained smoking reductions (50% reduction) do not reduce cancer or cardiac disease risk (Tverdall and Bjartveit, 2006).
Biobehavioural Vulnerability Factors to Tobacco Addiction in Schizophrenia

- Biochemical (reduced nAChR levels, higher baseline nicotine levels in Sz versus Controls)
- Genetic ($\alpha_7$ nAChR, $\alpha_3$ nAChR, COMT, DISC 1, Reelin)
- Behavioral (deficits in reinforcement/reward)
- Neurocognitive (neurophysiological/neuropsychological)

Wing, VC et al., 2012. Ann. NY Acad. Sci. 1248-89-106
Lower $\beta_2^*$-nAChRs in smokers with schizophrenia as compared to controls

D’Souza, DC, Esterlis, I. et al. (2012). Am. J. Psychiatry
Behavioral Factors – Mecamylamine Effects on Reinforcement, Consumption and Relapse

Topography – Puff Volume

*\( p < 0.05 \) vs. PLO

Consumption (Cigarettes/Session)

*\( p < 0.05 \) vs. PLO

Smoking Cue-Reactivity

*\( p < 0.05 \) vs 10 mg/day

McKee et al. (2009). Schizophrenia Res.
Fonder et al. (2005). Biol. Psychiatry
Effects of Abstinence on Visuospatial Working Memory (VSWM) in Smokers with Schizophrenia

Selective Enhancement of VSWM by Cigarette Smoking in Schizophrenia: Blockade by Mecamylamine

\[ F = 10.65, \text{ df} = 2,128, p < 0.01 \]

Deficits in Frontal-Executive Performance Predict Smoking Cessation Failure in Schizophrenia


Cortical Dopamine Function and Spatial Working Memory

George, T.P. et al., 2003, APPI
Atypical Versus Typical Antipsychotic Drugs and Nicotine Patch for Smoking Cessation in Schizophrenia (N=45)

Combination of Transdermal Nicotine and Bupropion SR is Superior to Placebo + Patch for Smoking Cessation in Schizophrenia (N=58)

Fisher’s Exact Test + p = 0.056 * p < 0.05 # p=0.11

Varenicline (Champix®)

- An $\alpha_4\beta_2$-selective nAChR partial agonist
- Approved by the FDA in May, 2006 and by Health Canada in April, 2007.
- In Phase III clinical trials, demonstrated superiority to both bupropion SR and placebo in continuous abstinence outcomes (Gonzalez et al., 2006, Jorenby et al., 2006)
- Prevents smoking-relapse with treatment up to 24 weeks (Tonstad et al., 2006).
- Dosing regimen is 0.5 mg qd x 3 days, then 0.5 mg bid x 4 days, then up to 1.0 mg bid for 12 weeks, with a label to extend treatment to 24 weeks as necessary.
Varenicline – Side Effects

- Main side effects are nicotine-like: Nausea (~30%), insomnia, headache and abnormal dreams.

- Black Box warnings issued by FDA, Health Canada and EMEA regarding anecdotal reports of treatment-emergent suicidality, homocidality, aggression, psychosis and mania – needs further study.
<table>
<thead>
<tr>
<th>Metabolized by CYP 1A2/3A4</th>
<th>Not Metabolized</th>
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<tbody>
<tr>
<td>Clozapine</td>
<td>Risperidone</td>
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<tr>
<td>Olanzapine</td>
<td>Ziprasidone</td>
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<tr>
<td>Haloperidol</td>
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<td>Chlorpromazine</td>
<td>Quetiapine</td>
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<tr>
<td>Caffeine</td>
<td>Bupropion</td>
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<td>SSRI’s</td>
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Varenicline and Psychiatric Populations

- Several case reports both published (Freedman, 2007; Kohen and Kremen, 2007) and unpublished (FDA Medwatch) implicating varenicline in neuropsychiatric treatment-emergent adverse events (TEAEs), including suicidality, homicidality, psychosis and mania (O’Malley, 2010).

- However, clinical studies comparing Psychiatric Hx+ to Hx- smokers in varenicline treatment suggest that treatment outcomes and adverse events are comparable (e.g. Stapleton et al., 2008; McClure et al., 2010).

- Recent controlled studies support its safety and efficacy in schizophrenia, , including in abstinence-initiation (Williams et al., 2012. J. Clin. Psychiatry; Anthenelli, RM et al. 2016 Lancet) and relapse-prevention (Evins et al., 2014. JAMA) studies.

- Four studies suggests its safety and efficacy in smokers with bipolar disorder (Weinberger et al., 2008; Wu et al., 2012; Frye et al., 2013; Chengappa et al., 2014)
Varenicline for Smoking Cessation in People with Schizophrenia (N=127)

OR: 4.74 (95% CI: 1.03, 21.78)  
\( p=0.046 \)

OR: 6.18 (95% CI: 0.75, 50.71)  
\( p=0.09 \)

Analysis population = ITT minus 1 subject randomized to varenicline who did not receive treatment

Varenicline Effects on Positive and Negative Symptoms in Smokers with Schizophrenia

EAGLES Study – Randomized Comparison of Varenicline, Bupropion SR, Nicotine Patch and Placebo for Smoking Cessation in Mentally Ill versus Non-Mentally Ill Smokers (N=8144)

FIGURE 1: Algorithm for Assessment and Treatment of Co-Morbid Tobacco Smokers

Evaluation of the Resistant Tobacco Smoker

(Consider a Co-Morbid SUD or PD)

Treat the Co-Morbid SUD, PD or Co-Morbid SUD/PD

Readiness to Change Tobacco Use (Yes/No)

If No, Brief Motivational Intervention

Nicotine Replacement and/or Bupropion SR or Varenicline + Behavioral Therapies. Monitor for psychiatric symptom and/or drug relapse with smoking cessation

If Yes, Proceed to Tobacco Treatment

Stimulates the cortex by trains of magnetic pulses.

Frequencies of 1 to 50Hz

rTMS has recently been used to treat neuropsychiatric disorders (e.g. depression, schizophrenia, parkinson’s disease)
rTMS reduces tobacco cravings in patients with schizophrenia