Project TEACH

Smoking Cessation For People With Schizophrenia

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Project ECHO®
Outline

1) What is behind the high comorbidity between Schizophrenia & Nicotine Dependence

2) Need for special treatment approach?

3) Any impact from smoking cessation on patients’ symptoms or stability?
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Background

- Schizophrenia patients show poorer cognitive performance and higher rates of smoking (1,2)

- Smoking has been considered a potential attempt to self-medicate and/or to partially counteract motor & cognitive side effects of certain antipsychotic medications (3,4)

- Cigarette smoking may reduce psychiatric symptoms and lessen antipsychotic-induced extra-pyramidal symptoms (4)

Background (2)

- Patients with schizophrenia have higher rates of tobacco use 80-90% (1) while in the general population in 2014 smoking level was at 16.8%

- Schizophrenia patients who are smokers are thought to have better cognitive performance

Background (3)

- How about the effects of smoking in treatment-resistant schizophrenia (TRS) patients?

- Smoker TRS patients had significantly higher scores on positive & negative syndrome scale (PANSS), & Neg. Symptoms Scale. They performed worse than nonsmokers TRS on problem-solving and other cognitive tasks (1)

1) Felice Iasevoli, Raffaele Balletta, Valentina Gilardi, Sara Giordano, and Andrea de Bartolomeis. Tobacco smoking in treatment-resistant schizophrenia patients is associated with impaired cognitive functioning, more severe negative symptoms, and poorer social adjustment. Neuropsychiatr Dis Treat. 2013; 9: 1113–1120. Published online 2013 Aug 7. doi: 10.2147/NDT.S47571 PMCID: PMC3742345
Shared Neurobiological Substrate

- A shared neurobiological substrate, ie, aberrant functioning of nicotinic cholinergic transmission, suggested to underlie both susceptibility to psychosis and vulnerability to smoking (1)

- Nicotine has been demonstrated to increase dopamine release in mesolimbic and mesocortical systems, (2-4) possibly underlying the cognitive-enhancing properties of smoking
Dopamine Pathways

- Thalamus
- Frontal cortex
- Hypothalamus
- Substantia Nigra

- Red: Dopamine pathway 1 (Parkinson's)
- Green: Dopamine pathway 2 (Schizophrenia)
Shared Neurobiological Substrate (2)

- Consistent with this view, deficits in $\alpha_7$ as well as in $\alpha_4\beta_2$ nicotinic receptors have been associated with cognitive impairment in schizophrenia patients (1,2)

- Nicotine administration to schizophrenia patients has been reported to improve several cognitive tasks that are usually found to be impaired, i.e. attention & working memory (3,4)

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For the patients who are unwilling or unable to quit, a smoking reduction approach may have benefits, with NRTs like the nicotine patch (1).

A meta-analysis suggested that bupropion is a safe medication smoking cessation with schizophrenia, although its effectiveness is inconclusive (2).

Smoking Cessation & Schizophrenia (2)
Bupropion + Patch

- Bupropion with nicotine patch were significantly more likely to achieve continuous smoking abstinence than patch alone.

- Importantly, the combination was well tolerated by smokers with schizophrenia and did not alter positive or negative symptoms (1).

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Smoking Cessation & Schizophrenia (3)
Bupropion + CBT

- Bupropion with CBT were more likely to increase abstinence a week after the quit date, as well as four weeks of continuous abstinence. However, high relapse rate were found at the end of treatment.

- Treatment with bupropion displayed a trend towards improvement in depressive & negative symptoms (1)

Smoking Cessation & Schizophrenia (4) Antipsychotics

- Haloperidol has been shown to increase smoking (1)

- Atypical antipsychotics combined with a nicotine patch had an enhanced rate of smoking cessation (2)

- Recent study determined that clozapine had no significant effect on smoking cessation (3)


Tony George et al. in (2002) showed that atypical antipsychotic medications: clozapine, risperidone, or olanzapine along with bupropion HCl did enhance smoking cessation outcomes when compared to placebo.

Smoking Cessation & Schizophrenia Combination Meds, Extended Tx & H. Visits

- Most recent study, Aug. 2016 in NTR:
  34 smokers with schizophrenia randomized to either COMB-EXT with Home Visits (HV), COMB-EXT without HV, or Tx as usual (TAU) (1)

- COMB-EXT: Group CBT + bupropion, nicotine patch, and nicotine lozenge, within 2 weeks and for 26 weekly visits.

Smoking Cessation & Schizophrenia
Combination Meds, Extended Tx & H. Visits

- HV: biweekly visits to the home, assessment of secondhand smoke (SHS) exposure and brief behavioral therapy with participants and others in the home environment.

- TAU consisted of group CBT plus serial single or combination medication trials as per standard care.

COMB-EXT (with or without HV) had greater reductions in CPD than those treated with TAU (both ps < .01).

7-day PPA for the three groups were 45%, 20%, and 8%, respectively, which was significantly higher for COMB-EXT plus HV than TAU ($\chi^2(1) = 4.8$, $p = .03$).
Effect of Combination Extended Treatment (COMB-EXT) with or without home visits (HV) compared to treatment as usual (TAU) on measures of smoking behavior.

Arthur L. Brody et al. Nicotine Tob Res 2016;ntr.ntw190

Published by Oxford University Press on behalf of the Society for Research on Nicotine and Tobacco 2016. This work is written by (a) US Government employee(s) and is in the public domain in the US.
Cognitive function in Schizophrenia & Varenicline

- Varenicline improved executive function and reduced startle reactivity, regardless of smoking status in subjects with schizophrenia (1)

- Varenicline led to some cognitive improvement for list learning, list recall, and language index (2)

In a multisite study, varenicline was well tolerated, with no evidence of exacerbation of symptoms, and was associated with significantly higher smoking cessation rates 19% versus placebo 4.7% at 12 w. (1)

In a large study (53 subjects), Varenicline + CBT for 12-weeks: 60.4% attained 14-day PPA (2)


2) Dutra SJ, Stoeckel LE, Carlini SV, Pizzagalli DA, Evins AE. Varenicline as a smoking cessation aide in schizophrenia: effects on smoking behavior and reward sensitivity. Psychopharmacology (Berl) 2012;219:25–3
Another study with varenicline in schizophrenia showed patients with lower baseline symptoms of affective flattening (more typical affect) were more likely to achieve smoking abstinence, and demonstrated larger increases in reward sensitivity during treatment (1)

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Impact of Smoking Cessation on symptoms or stability?

None of the published reports have found exacerbation of symptoms of psychosis or other symptoms in subjects diagnosed with schizophrenia after they quit smoking with any of the currently available medications.

Stapleton et. al. (2008) did not find exacerbation of symptoms of mental illness in subjects diagnosed with depression, bipolar disorder, psychosis, psychosis and depression, and eating disorders following treatment with varenicline combined with group support.

Take Home Points

- Schizophrenia patients have a complex biology and interplay with nicotine receptors, that has an impact on manifestation of psychosis symptoms and cognitive functioning.

- Patch and bupropion are safe but do not produce a robust abstinence when used alone.

- In combination: Bupropion, patch and CBT would have a higher sustained abstinence in particular if extended Tx and adding Home visits.
Take Home Points (2)

- Varenicline has potential for improving some of the cognitive functions in schizophrenia
- Varenicline significantly improves abstinence, although lower rates than general population
- Smoking cessation with any of the available medications do not have an impact on psych symptoms among patients with schizophrenia