Smoking and drug interactions in psychiatric patients

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INTRODUCTION

There is no debate as to the negative impact of cigarette smoking on one's health. Yet, in schizophrenic patients, breaking this habit should be monitored to avoid complications caused by increased blood serum levels of specific drugs.

Schizophrenic patients have been reported to have a higher prevalence of ever-smoking than the general population. According to the National Comorbidity Survey , nearly 50% of patients with previous or current nonaffective psychosis are ever-smokers [de Leon J, Diaz FJ. A Schizophr Res. 2005 Jul 15].

Clozapine is an atypical antipsychotic used in the treatment of therapy-resistant schizophrenia. Although it provides effective treatment, its use is limited by the dangerous side effect of agranulocytosis, requiring close monitoring of white blood cells count. Despite this fact, clozapine usage is on the rise because it is often the only effective treatment for therapy-resistant schizophrenia.

The drug is metabolized extensively by cytochrome P450 isoenzyme (CYP) 1A2. In parallel, polycyclic aromatic hydrocarbons (PAHs) present in cigarette smoke are considered to be inducers of CYP 1A2. Therefore, smoking while taking clozapine can potentially decrease the medication levels and lead to decreased efficacy, while smoking cessation can potentially lead to increased levels and possible toxicity.

The following case study describes a case where changes in smoking status altered serum drug concentrations, thereby affecting the patient's wellbeing.

CASE ESSENTIALS

Age:	58
Gender:	Woman
Medical Conditions:	Hypertension, Schizophrenia and Type 2 Diabetes
Patient-specific factors:	Smoking (up to 40 cigarettes a day)

CASE REPORT

A 58 years old woman suffering from hypertension, schizophrenia and type 2 diabetes, and living in a group home, had been treated with clozapine for three years. Before hospital admission, she has been taking a daily dose of 700 mg for several months, with a plasma level of clozapine of 459 µg/l, well within the therapeutic range of 350-700 µg/l. In her intermittent smoking periods, this woman was smoking up to 40 cigarettes a day. She stopped smoking several weeks before admitting to the hospital. Her daily medications included clozapine, citalopram, atorvastatin, metformin, nifedipine and ramipril. She arrived at the emergency department presenting psychotic symptoms and anxiety and was admitted to a nonsmoking inpatient psychiatric facility. She had a history of multiple psychiatric hospitalizations, and over the week prior to admission, had been suffering from increasing auditory and visual hallucinations and paranoia. The patient had been compliant with hematologic monitoring with clozapine for over three years based on monthly hematologic monitoring. On admission, she was

noted to have tachycardia (HR 105 bpm), hypotension (85/50mmHg) and a BMI of 36 (obese); all other labs and vital signs were within normal range. Additionally, she reported auditory hallucinations, paranoid delusions, and persecutory delusions, with voices threatening to kill her. The initial treatment prescribed by the admitting physician included the same dose of clozapine she was taking regularly.

On her second day in the hospital, she reported dizziness while standing. A clozapine level test was ordered, and orthostatic vital signs were monitored to gain clarity regarding compliance with clozapine before admission, as well as to resolve suspicion regarding clozapine-induced orthostatic hypotension and tachycardia that may have been related to the 700 mg dose. The patient had displayed orthostatic hypotension and tachycardia for several days, but the sample was taken 2 hours post-dose and was inappropriate for testing the clozapine level (it wasn't at trough levels). Negative cardiac enzymes and an EKG showing sinus tachycardia were thought to rule out clozapine myocarditis.

HOW USING SEEGNAL COULD HAVE INFLUENCED PATIENT TREATMENT AND PREVENT SIDE EFFECTS

Several studies indicate that smoking could decrease levels of clozapine serum levels by up to 58%, as a sensitive substrate of CYP1A2 [van der Weide J, Steijns LS, van Weelden MJ., Pharmacogenetics. 2003].

If the clinician would have used Seegnal, a smart, patient-specific off-the-shelf software, during hospital admission, Seegnal would have immediately alerted the physician regarding smoking as a significant patient factor that influences the suggested drug therapy. The clinician would also be able to see that once smoking inductive effect ceases, clozapine serum levels could increase significantly, and dosage modification should be made to prevent clozapine toxicity.

As a result of tests performed, the interaction between clozapine and cigarette smoking was identified and the dose of clozapine was decreased to 100 mg every morning and 300 mg at bedtime. Additionally, propranolol 20 mg PO three times a day was initiated for dealing with the clozapine-induced tachycardia. The hypotension and tachycardia gradually subsided and were resolved by Day 6 of admission. The patient showed gradual improvement, including reported reduction of auditory hallucinations and improvement in activities of daily living (ADLs), with less isolation and increased spontaneous speech. Notably, the patient had continually asked throughout the course of hospitalization if she could smoke and smiled for the first time on the day of discharge as she could smoke cigarettes again. Taking into consideration the resumption of smoking on discharge, she was discharged with gradual increase in clozapine dosage, to slowly balance enzyme induction effect.

DRUG-PATIENT FACTOR INTERACTIONS PLAY A KEY ROLE IN EVERYDAY PATIENT CARE

Drug-patient factor interactions can have significant impact on patient wellbeing and outcome. Smoking can potentially have a significant effect on a patient's reaction to medication therapy. The interaction of smoking with CYP1A2 substrates, such as theophylline, clozapine, olanzapine, duloxetine and others may result in serious clinical consequences for patients who are taking these medications regularly.

ABOUT SEEGNAL

Seegnal eHealth Ltd. was established with the goal of globally disrupting the clinician-medication-patient value chain by introducing revolutionary concepts, new knowledge, and advanced technologies, generating both value and safety.

Seegnal is a smart and intuitive clinical decision support platform that empowers clinicians to quickly and effectively manage and resolve patient-specific Drug-Related Problems (DRPs - the 4th leading cause of death in the US alone).

Seegnal interfaces with the EMR at the point of care and harnesses the widest scope of DRP-related information, generating an additional 50% of unique data (which legacy systems either don't recognize or address), while delivering groundbreaking accuracy (sensitivity and specificity) of about 95%.

The platform diminishes alert fatigue (~ 6% alert load vs. legacy systems) and is intuitive and easy to use, requiring only 5-10 seconds for DRP detection, prioritization, and resolution.

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