Welcome to the webinar sponsored by: The IDPH Office of Problem Gambling Prevention and Treatment
Parkinson’s/RLS Medication Affecting Increase in Problem Gambling
Presented by:
Dr. Anhar Hassan
April 8, 2015
12N – 1:30 pm, Central Time Zone
Slide handouts available at: Parkinson’s/RLS PPT slide handouts
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How to participate today:
There are several ways we will ask you to participate during the presentation:
• **Question and Answer box**: type your question or comment in this box.
• **Polling Questions**: by clicking on the answer(s) in the polling box.

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Session Goals:
• **To be aware of the medications treating Parkinson’s disease/restless leg syndrome that cause problem gambling (and other compulsive behaviors)**
• **To be familiar with other risk factors (in addition to medications) that can cause these behaviors.**
• **To be aware of the treatment approach if these problems occur**

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Agenda for this webinar

- 12:00-12:05 – Introduction
- 12:05-1:15 – Training Session
- 1:15-1:30 – Question and Answer
- 1:30 pm – end of session – Please complete survey at the end of this webinar

About the presenter:

Dr. Anhar Hassan is a Mayo Clinic neurologist with specialist training in movement disorders and electrophysiology. She has published over 20 original papers and 1 book chapter. Her research interests include impulse control disorders due to medication-treatment of Parkinson’s disease.

Talk Outline

1. Medications for Parkinson’s disease/restless leg syndrome that cause problem gambling ( + other compulsive behaviors)

2. Review other risk factors for these behaviors.

3. Treatment of problem gambling ( + other behaviors)
Talk Outline

1. Medications for Parkinson’s disease/restless leg syndrome that cause problem gambling (+ other compulsive behaviors)

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Polling Question 1

Parkinson Disease (PD)

A progressive neurological disorder of:

- Tremor
- Stiffness (Rigidity)
- Slowness of movement (bradykinesia)
- Loss of balance/falls (postural instability) (later on)

- Common, ~1% of Americans
- Caused by loss of dopamine cells in the brainstem.
Restless Legs Syndrome (RLS) (Willis-Ekbom Disease)

• An unpleasant sensation in the legs (or arms), “creeping”, “crawling”, “tingling”
• Worse in the evening or in bed, relieved by moving legs and worse holding still
• Very common, 5-10% US population
• Cause is unknown, could be related to abnormal brain dopamine function

Links between PD and RLS

• RLS is more common in people with PD than those without PD
• Both PD and RLS can be treated by:
  1. boosting brain dopamine levels
     e.g. levodopa
  2. stimulating dopamine receptors (without increasing dopamine levels)
     e.g. dopamine agonists

PD Treatments

• Levodopa (Sinemet), since 1950s
• Dopamine agonists, since 1970s
  – 1970s: Older drugs e.g. bromocriptine, pergolide
  – Late 1990s: Newer drugs e.g. pramipexole (Mirapex), ropinirole (Requip), rotigotine patch (Neupro)
• Many other medications - selegeline (Eldepryl), rasagiline (Azilect), amantadine (Symmetryl), COMT inhibitors (Comtan), Stalevo, apomorphine (Apokyn)
RLS Treatments

- Levodopa – eventually worsens RLS, so not recommended anymore
- Dopamine agonists (pramipexole, ropinirole, rotigotine patch)
- Gabapentin, pregabalin
- Opiates e.g. codeine

Ok, so where does problem gambling fit in?

Impulse Control Disorders (ICDs)

- Pathologic (problem) gambling
- Pathologic hypersexuality
- Binge eating
- Compulsive spending / shopping

Occurs in the normal population
Can be devastating, ruin finances, reputation, family/ personal relationships
Problem Gambling in PD

- In 2000, cases of new problem gambling in PD patients were published (Molina 2000, Seedat 2000, Schwindtner 2001)
- In 2003, 9 cases were reported at one clinic amongst 1,884 PD patients. Thought to be rare, ~ 0.5% frequency (Driver-Dunckley 2003)
- In mid-late 2000s, higher frequencies of cases were reported, ~3-5%

Then other problem behaviors were noted....

- Pathologic hypersexuality (Budd 2005, Weintraub 2006, Voon 2006)
- Binge eating (Ninemerg 2005)
- Compulsive hobbying/punding (Fisano 2006)
- Single case reports: “walkabout”, hoarding, impulsive smoking, reckless driving

Later studies found ICDs were common - 17% (1 in 6) of PD patients taking dopamine agonists. (Weintraub 2010)
- One study reported as high as 40%.
- Usually 1-2 behaviors, rarely more than this
  - Males: gambling, hypersexuality
  - Females: binge eating, compulsive shopping
What about problem gambling and behaviors in RLS?

- First cases reported in 2007 by Mayo Clinic neurology sleep physicians (Tippman-Peikert 2007)
- 2010 study, ~17% ICDs on dopamine agonists (Cornelius 2010)
  - Pathologic gambling
  - Pathologic hypersexuality
  - Binge eating
  - Compulsive shopping
  - Punding

What was the common link?

- Dopamine agonist medications

Which of the dopamine agonists?

- Pramipexole and ropinirole
  - Also: Rotigotine patch (Neupro)
    Older dopamine agonists (e.g. bromocriptine, pergolide)
Have they caused problem behaviors (ICDs) in other conditions?

- Yes, dopamine agonists caused ICDs when prescribed for other conditions
  - Fibromyalgia, pituitary tumors, multiple system atrophy (MSA)

Frequency of behaviors

<table>
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<th>Current ICD2</th>
<th>OR 95% CI</th>
<th>P value</th>
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</table>


The risk increases with the dose

- Overall ~17% (1 in 6)
- 24% (1 in 4), if taking a medium (target) dose
- 30% (1 in 3), if taking a high dose.

(Hassan, Park Rel Disord 2011)
The behavior(s) can start any time.

- Can start at low dose
- Can start after increasing the dose
- Can start after taking a steady dose of medication for several years
- On average ~ 2 years of medication.

Polling Question 2

Talk Outline

1. Medications for Parkinson’s disease/restless leg syndrome that cause problem gambling (+ other compulsive behaviors)

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3. Treatment of problem gambling (+ other behaviors)
Polling Question 3

Polling Question 4

• Are there other risk factors for problem gambling (+ other behaviors) in PD and RLS?
1. Patient
- PD
- Male, younger age, early-onset PD
- Personal/family history of ICDs or substance/alcohol abuse
- Smoking
- Major depression, anxiety, OCD
- Novelty seeking, impulsive
- Unmarried
- REM sleep disorder
- Deep Brain Stimulation – subthalamic nucleus (STN)
- RLS
- Depression?

2. Medication
PD
- Dopamine agonist dose
- Taking levodopa with dopamine agonist
- Apomorphine
- Selegiline, rasagiline
- Aripiprazole
- Modafinil
- RLS
- Can occur at low dose of dopamine agonist

3. Genetic
PD
- Several genetic variants in dopamine, serotonin, and glutamate receptors are linked to ICD risk.
- Possible - Needs further study
- RLS
- No studies
4/7/2015

Polling Question 5

Polling Question 6

Talk Outline

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Polling Question 7

Prevention

• Screen patients at risk

• Education for patient and family

• Follow-up surveillance at each visit

Black box warning?
Treatment

• Reduce or stop the dopamine agonist

• Works for most patients

Treatment

• If PD or RLS symptoms get worse, can substitute another medication
  – e.g. levodopa, entacapone, amantadine* in PD
  – e.g. gabapentin, pregabalin in RLS

*Conflicting evidence if ICDs worse

Treatment

• Control environment
  – Credit card limit
  – Firewall
  – PD or RLS support groups
  – Gamblers Anonymous
  – Cognitive behavioral therapy
In a few cases....

• The patient cannot stop dopamine agonist
• Behaviors continue despite stopping

1. Consider Deep Brain Stimulation for PD patients
   – Allows reduction of medication
   – Caution: STN DBS can provoke or worsen ICDs

2. Specific medications to treat ICDs
   • This is experimental only, and off-label use
   • Antipsychotics
     – Clozapine, quetiapine (Risperidone, Quetiapine, Olanzapine can worsen PD)
   • Anti-epileptic medications
     – Valproate, Zonisamide, Topiramate, Carbamazepine
   • Duopa (enteral levodopa/carbidopa infusion)
   • Naltrexone
   • Antidepressants (SSRIs) – fluvoxamine, paroxetine

Management

• Follow-up patient
  – Remission or significant improvement in 73-83%, when dose reduced or stopped
  – Maintained for 21-49 months

• The longer-term outcome is not known
Polling Question 8

Future directions

- Understand what is happening in the brain
- Identify a biomarker for gambling /ICDs
  - Clinical / genetic factors
- Personalized medicine
  - Predict which patients are vulnerable.
  - Avoid prescribing dopamine agonists in these patients.

Take-home points

- Dopamine agonists are the main risk factor for problem gambling and other impulse control disorders
- Stopping the medication should improve the gambling or other behavior
- Notify your health care provider if you notice new behaviors with dopamine agonists
Question and Answer

We will now take time to answer any questions that have been submitted.

Final Questions and Answers

We will now take time to answer any final questions.

Thank you for attending!

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