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HDSA encourages all attendees to consult with their primary care provider, neurologist or other healthcare provider about any advice, exercise, medication, treatment, nutritional supplement or regimen that may have been mentioned as part of any presentation.
Presenter Disclosures

Victor Sung, MD

The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

Served as a Consultant for Lundbeck, and the use of their product(s) will be discussed in this talk.
Managing Movements

• Summary of Motor Symptoms
• Current Treatments
  – FDA-approved
  – Non FDA-approved
  – Summary of Scientific Data
• Multi-drug therapy
• Drug Interactions
• Real World Scenarios
• Summary
Introduction

• Though we don’t have a cure, there IS HOPE!
• Contrary to the impressions of many physicians, the motor symptoms of HD CAN be adequately managed!
Motor Symptoms of HD
Motor Symptoms of HD

• **Importance**
  – Prior to genetic testing (CAG repeat) availability, HD diagnosed by *motor* symptoms
  – Even now, onset of disease is defined by onset of *motor* symptoms

• **Categorization**
  – By stage of disease (early, middle, late)
  – By type of movement (chorea, dystonia, tics, myoclonus, rigidity, etc)
Types of Motor Symptoms

• Abnormal Involuntary Movements
  – Chorea
  – Dystonia
  – Tics / myoclonus

• Parkinsonism (Rigidity / bradykinesia)

• Speech / Swallowing Problems

• Balance/Walking Problems & Falls

• Eye Movement Abnormalities
Stages of Motor Symptoms

• **Early Stage HD**
  – Changes in coordination
    • Less control of handwriting
    • More difficulty with tasks like driving
  – Mild beginning of chorea
    • Fidgeting
    • Restlessness
  – Myoclonus / Tics
    • Irregular, sudden jerks
    • Facial twitch
Stages of Motor Symptoms

- **Middle Stage HD**
  - Chorea
    - Arms – dropping items
    - Legs – affecting gait
    - Trunk – writhing movements
  - Balance / walking problems
    - Stumbling, near falls
  - Speech / swallowing problems
    - Slurring of speech, coughing with food
  - Slow reaction time
Stages of Motor Symptoms

• Late Stage HD
  – Parkinsonism
    • Rigidity (stiffness of muscles)
    • Bradykinesia (slowness of movement)
  – Dystonia
  – Severe speech / swallowing problems
    • Unintelligible speech
    • Choking
  – Loss of independence for ambulation
  – Inability to perform activities of daily living
Current Treatments for Motor Symptoms of HD
# Motor Symptoms of HD

<table>
<thead>
<tr>
<th>Specific Medical Treatments Available</th>
<th>NO Specific Medical Treatment Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chorea</td>
<td>Speech problems</td>
</tr>
<tr>
<td>Dystonia</td>
<td>Swallowing problems</td>
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<tr>
<td>Tics</td>
<td>Balance / Walking problems</td>
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<tr>
<td>Myoclonus</td>
<td>Falls</td>
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<tr>
<td>Parkinsonism</td>
<td>Eye Movement Abnormalities</td>
</tr>
</tbody>
</table>
Why Bother Treating These?

• Have you heard that argument?
  – The left column is less debilitating than the right column

• Because…
  – There is no ‘magic’ walking / swallowing / coordination improvement pill…and likely never will be!
  – These abnormal movements CAN be treated and DO contribute significantly to the other items on the right
  – Doing nothing is NOT an option – what do we have to lose??

Huntington’s Disease Society of America
Why Do Treatable Symptoms Often Go Untreated?

• My personal experience with many patients coming to me on NO treatments
• Patients may not recognize symptoms like chorea
  – Gradual onset
  – May not consciously accept that they have a movement disorder
  – Not bothered by it
  – Loss of insight
Caregiver Opportunity

Caregivers:

• In some situations, caregivers may be more aware of HD motor symptoms than patient

• Speak up to the care provider on behalf of your loved one
  • Even if it requires separate discussion away from loved one

Patients and family input/corroborated can build better picture of patient’s social activities and disease burden
Current Medical Treatments – Abnormal Involuntary Movements

• Chorea
  – Tetrabenazine (Xenazine)
    • FDA-approved in August 2008 for HD chorea
    • Data comes from Huntington’s Study Group trial called Tetra-HD
    • Not stocked in retail pharmacies
Tetrabenazine for HD

- **Tetra-HD**
  - 12-week randomized, double-blind, placebo-controlled multicenter trial
  - 16 Huntington's Study Group sites in the US
  - 84 Patients Enrolled
    - 54 randomized to tetrabenazine
    - 30 randomized to placebo
  - **Results**: Mean 23.5% reduction in chorea that returned to baseline during washout
  - Avg. dose in trial was 75mg/day
Tetrabenazine for HD

• What about the “black box” warning for depression / suicide?
  – In Tetra-HD, 1 suicide, 4 with worsened depression
  – My clinical experience

• What about the cost?
  – Very expensive, but usually covered by insurance
  – My experience with Reach Program
  – Awesome work of Caring Voice Coalition

• Does it really work?
  – My patient stories…
Current Medical Treatments – Abnormal Involuntary Movements

• Chorea
  – Typical antipsychotics
    • **High potency**: haloperidol, fluphenazine, prochlorperazine
    • **Medium potency**: perphenazine, thiothixene, loxapine, trifluoperazine
    • **Low potency**: chlorpromazine, thioridazine
Current Medical Treatments –
Abnormal Involuntary Movements

• Chorea
  – Typical antipsychotics
    • The higher the potency, the greater the effect on motor symptoms and less side effects
    • **Use of benztropine (Cogentin) is counter-productive in HD as it blocks the motor effects of the antipsychotic!**
Current Medical Treatments – Abnormal Involuntary Movements

• Chorea
  – Atypical antipsychotics
    • Risperidone, olanzapine, ziprasidone, aripiprazole
    • Quetiapine, clozapine (do NOT help chorea)
    • Black box warning for early death in elderly
Typicals vs. Atypicals

• **Efficacy**
  – Generally, typicals more potent for motor symptoms
  – Equal efficacy for psychotic symptoms

• **Cost**
  – Typical: Haloperidol, fluphenazine, prochlorperazine, thioridiazine, thiothixene all on $4 List
  – Most atypicals branded
## Typical vs. Atypical – Side Effects

<table>
<thead>
<tr>
<th>Typical</th>
<th>Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Weight Gain</td>
<td>++ Weight Gain / Metabolic Syndrome **</td>
</tr>
<tr>
<td>++ Tardive dyskinesia**</td>
<td>+/- Tardive Dyskinesia</td>
</tr>
<tr>
<td>+/- Sedation</td>
<td>++ Sedation</td>
</tr>
<tr>
<td>+ Dry mouth</td>
<td>Dry mouth</td>
</tr>
<tr>
<td>+ Orthostatic hypotension</td>
<td>Orthostatic hypotension</td>
</tr>
<tr>
<td>+ Parkinsonism</td>
<td>Parkinsonism</td>
</tr>
<tr>
<td>+ Dystonia</td>
<td>Dystonia</td>
</tr>
</tbody>
</table>
Other Treatments

- Amantadine
  - One study using 400mg/day showed some reduction in chorea
  - One study using 300mg/day showed no benefit
  - Overall well tolerated

- Benzodiazepines
  - Not directly beneficial but decrease stress amplification component
Current Medical Treatments – Abnormal Involuntary Movements

- **Dystonia**
  - Botulinum toxin injections if focal

- **Parkinsonism (rigidity/bradykinesia)**
  - Can use small dose carbidopa/levodopa

- **Myoclonus / Tics**
  - Benzodiazepines
  - Anticonvulsants (topiramate, levetiracetam)
  - Clonidine
Other Therapies

• Healthy, balanced diet
  – High protein or supplements (creatine/CoQ10)
• Exercise
• Physical Therapy, Occupational Therapy, Speech Therapy
  – All shown to be beneficial
    • Cost can be a barrier for some
  – Importance of a multidisciplinary clinic if available
Families affected by HD may need a high degree of support from a multidisciplinary healthcare team\(^1\)

Surgical Treatments

• Deep Brain Stimulation Surgery
  – For medically refractory chorea (and possibly dystonia, tics)
  – A few case reports
Multi-Drug Therapy
Multi-Drug Therapy

- Often not done out of fear of side effects
- Possible combinations
  - TBZ + typical antipsychotic
  - TBZ + atypical antipsychotic
  - Multiple antipsychotics (typical + atypical)
  - Any of above + Amantadine
  - Any of above + Benzodiazepine
Drug Interactions
Drug Interactions

• Typical antipsychotic + Tetrabenazine
  – Some can increase levels of tetrabenazine
  – In general, additive effects can cause more side effects (sedation, cardiac arrhythmias)

• Paroxetine or Fluoxetine + Tetrabenazine
  – Both are on $4 List, commonly used
  – When taken in combination with tetrabenazine, should HALF the dose of tetrabenazine
Drug Interactions

• Multiple antipsychotics
  – Typical + Atypical can be used with caution
  – In general, not recommended to use multiple typicals or multiple atypicals

• Decongestants
  – Many will increase levels of tetrabenazine and antipsychotics

• Coumadin
  – Surprisingly, no major drug interactions
Treatments on the Horizon for HD Movements

- SD-809 / Deuteration of tetrabenazine
  - Effectively, like an extended release tetrabenazine
  - Deuteration allows much lower total daily dose, may avoid some of current side effects
  - HSG-funded clinical trial to begin enrollment in July (more info at this meeting!)

First-HD
A Huntington Disease Research Trial
Treatments on the Horizon for HD Movements

- Pridopidine / ACR-16 / Huntexil
  - Dopamine stabilizer instead of depleter
  - Showed benefit in non-chorea motor symptoms of HD
  - Very low side effect profile at low doses
  - Rights purchased by Teva Neurosciences
Real World Scenarios
Real World Scenarios

- Very mild chorea on exam
  - Chorea doesn’t bother patient
  - Prominent depression, cries during exam, follows with a psychiatrist

- Mild-moderate chorea on exam, tripping/falls
  - On no treatment
  - Reports depression
  - No insurance, or Medicaid only from another state
Real World Scenarios

• Patient is on tetrabenazine 25mg 3x/day
  – What if chorea is better but now developing depression?
    • Options?

  – What if chorea still not better on that dose?
    • Options?
Real World Scenarios

• Primarily psychiatric symptoms, controlled on a typical antipsychotic for many years
  – Now beginning to develop uncomfortable movements in abdomen

• Some mild chorea on exam, problematic obsessive-compulsive symptoms
  – On no treatments
Summary
Bottom Line

- There IS hope – there ARE treatments that can help
- So what do I really do?
  - Push towards early treatment – why?
    - Is the alternative of doing nothing really better?
    - Analogy of chemotherapy for cancer
  - If pure motor symptoms, TBZ first
  - If motor symptoms but some depression, add SSRI first to stabilize then add TBZ
  - If equally mixed motor/psychiatric, antipsychotic first
  - Weigh typicals vs. atypicals based on side effects and cost
  - Rely heavily on my PT/OT/ST colleagues
References / Resources

• HD Buzz
  – http://www.hdbuzz.net

• Huntington’s Disease Drug Works Site:
  – http://hddrugworks.org

• HD Lighthouse
  – http://www.hdlf.org

• WEMOVE.org’s Free HD Caregiver Guide (PDF)
Acknowledgements

- HDSA / UAB Center of Excellence
- HD Patients and Families