Research Visits with the Prader-Willi Population

Brittany Machus, MA, CCRP
Children’s Minnesota
Sue Keams, BSN, MN
Seattle Children’s

Disclosures

Neither speaker has any disclosures to report.

Objectives

1. Describe the most common characteristics of someone with Prader-Willi Syndrome (PWS).

2. Identify differences between clinical care and research study visits that may have an impact on someone with PWS.

3. Discuss methods that can be used to help facilitate successful research visits with the PWS participant.
Review of Prader-Willi Syndrome (PWS)

- Chromosome 15q11-13
  - Paternal deletion: 70%
  - Uniparental disomy: 25%
  - Imprinting defect: 5%
- Occurs in approximately 1 in 12,000 to 15,000 births
- Most common genetic cause of obesity

Characteristics of PWS

- Almond shaped eyes
- Narrow bridge of nose, narrowing of forehead at temples
- Thin upper lip and upturned mouth
- Small hands and feet

Characteristics of PWS

- Low birth weight/poor feeding as infants
- Hypotonia
- Hyperphagia
- Slow metabolism
- Cognitive delays
- Obsessive/Compulsive behaviors (e.g. skin/rectal picking)
- Behavioral problems
- Short stature
Other Associated Problems

- Sleep issues: sleep apnea, hypersomulence
- Scoliosis
- Hypogonadism
- GI symptoms: gastroparesis, constipation, lack of vomiting
- Autism
- Hormone imbalances
- High pain tolerance

Hyperphagia

- Increased appetite begins in early childhood (~2-5 years old) and then rapidly increases
- Patients may steal food, forage through the trash, and eat non-food items
- Excessive eating can lead to death from severe obesity, choking, or stomach rupture
- Food is a constant source of perseveration

Hyperphagia is the #1 barrier to these patients living independently

Current Treatments

- Growth hormone: usually started after diagnosis (infancy)
- Other hormone deficiencies: testosterone, estrogen, thyroid
- Hypersomulence: Modafinil, Contrave, etc.
- Skin picking: n-acetylcysteine
- Psychiatric/behavioral issues: psychotropic medications
- Weight management: low calorie diet plus exercise

There is no cure for PWS and conventional weight management treatments have not been successful
Research in the PWS Population

- Few pharmacologic studies in the past

<table>
<thead>
<tr>
<th>Current Non-Medication Trials</th>
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</thead>
<tbody>
<tr>
<td>PATH for PWS</td>
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<tr>
<td>Parent-Focused Remote</td>
</tr>
<tr>
<td>Education to Enhance</td>
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<tr>
<td>Development (PRETENDS)</td>
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<tr>
<td>PWS Anxiety and Stress</td>
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<tr>
<td>Questionnaire (PADQ)</td>
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<tr>
<td>PWS Activity, Sleep and</td>
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<tr>
<td>Eating Pattern Pilot Study</td>
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<tr>
<td>Mindfulness-based intervention for hyperphagia in PWS</td>
</tr>
<tr>
<td>Web-based study of cognition</td>
</tr>
</tbody>
</table>

- First large trial to demonstrate statistically and clinically significant improvement in hyperphagia-related behaviors and weight loss
- Families were eager to join
- 108 patients enrolled
- 3 groups: 2 different doses of Beloranib and placebo
- 5 patients discontinued due to adverse events
- Unfortunately, 2 deaths lead to the trial being stopped

Current PWS Studies

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosage</th>
<th>Contraindications</th>
<th>Common Adverse Reactions</th>
<th>Unique Adverse Reactions</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beloranib</td>
<td>20 mg</td>
<td>No</td>
<td>Nausea, vomiting, diarrhea</td>
<td>NA</td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td>10 mg</td>
<td></td>
<td></td>
<td></td>
<td>Oral</td>
</tr>
</tbody>
</table>

McCandless, S. Diabetes Obes. Metab. 2017, 19: 1751-61

### Clinical Care Vs. Research Visits

<table>
<thead>
<tr>
<th>Clinical Care</th>
<th>Research</th>
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</thead>
<tbody>
<tr>
<td>Quarterly/semi-annual visits</td>
<td>Weekly/monthly, possibly with added travel</td>
</tr>
<tr>
<td>30-60 minutes (unless multiple providers)</td>
<td>1.5-6 hours or more</td>
</tr>
<tr>
<td>Routine structure/procedures</td>
<td>Visit structure varies</td>
</tr>
<tr>
<td>Known staff</td>
<td>Unfamiliar procedures (ECG, DEXA, etc.)</td>
</tr>
<tr>
<td>Established relationship</td>
<td>Procedures done multiple times</td>
</tr>
<tr>
<td></td>
<td>Unknown to staff/facility</td>
</tr>
</tbody>
</table>

### Clinical Care Vs. Research Visits

<table>
<thead>
<tr>
<th>Clinical Care</th>
<th>Research Visits</th>
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</thead>
<tbody>
<tr>
<td>Fasting not required</td>
<td>FASTING often required</td>
</tr>
<tr>
<td>“Need” driven</td>
<td>Protocol driven</td>
</tr>
<tr>
<td>Few transitions</td>
<td>Lots of transitions in single visit</td>
</tr>
<tr>
<td>Labs may not be required</td>
<td>Most participants must give assent/permission</td>
</tr>
</tbody>
</table>

**Hyperphagia**

- Set expectations on fasting/meal times before the visit
- Send consent prior to visit for guardian/caregiver review
- Get all fasting procedures done as soon as possible
- Be prepared, be efficient, be fast (and hope the blood draw goes well!)
**Tips for Successful Research Visits**

**Hyperphagia**
- Have family bring in their food
- Schedule meal breaks (follow typical food schedule if possible)
- Limit discussions about food
- Find distractions
- Be aware of surroundings: cafeteria, trash, staff lunches, etc.

**Tips for Successful Research Visits**

**Obsessive Compulsive Behaviors**

**Skin Picking**
- Use verbal cues
- Use distraction/redirection (coloring, puzzles, crafts)
- Find alternatives for wearing ID bands
- Cover lesions or ‘picking areas’ (clothing, bandages, Coban wrap, etc.)

**Perseveration**
- Re-direct and distract—be aware of your verbal or nonverbal feedback
- Introduce a different topic or procedure
- Provide a quiet break
- Don’t feed into repetitive questions

**Tips for Successful Research Visits**

**Obsessive Compulsive Behaviors**

- What you do at the first visit may establish participant’s expectations for the rest of the study
- Provide consistent staff, give notice if this changes
- Keep same routine order each visit if possible
- Provide adequate preparation for changes
- Plan ahead to limit schedule disruptions

SUCCESS!
### Tips for Successful Research Visits

#### Common Behavior Issues

- **Anxiety**
  - Be clear, break things down into smaller steps
  - Use visual schedule
  - Be positive
  - Child Life

- **Crying/meltdowns**
  - Provide a break if appropriate
  - Minimize sensory input
  - Be firm and remind patient of expectations
  - Respect Assent

- **Aggression**
  - Remain calm, set the tone
  - Provide a break

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#### Common Behavior Issues

- **Defiance/refusal to cooperate**
  - Set the expectations right away
  - Create a "new routine" around research
  - Offer minimal choices if possible
  - Don’t engage in power battle

- **Withdrawal/the silent treatment**
  - Try to engage patient with their interests
  - Don’t withdraw in return
  - Keep schedule moving

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#### Developmental Delay

- **Obtaining meaningful assent**
- May not know developmental level prior to visit
- Send assent home prior to visit
- Don’t assume participant understands routine requests
- Provide developmentally appropriate distractions, rewards, explanations
Tips for Successful Research Visits

**Obesity**
- May be too large for certain procedures
- May be a challenge to position for measurements
- Blood draws may be very difficult.
- Have patient hydrate 1-2 days prior to visit
- Warm venipuncture site if tolerated
- Use longer needles/PIV needle
- Explain multiple pokes may be needed. Consider an IV if serial draws required.

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**Scoliosis**
- Heights may be difficult to obtain consistent heights
- Allow adequate time for positioning, triplicate collection
- Use at least two people
- Consider lying down

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**Questionnaires**
- Parent or guardian completes questionnaires
- Provide activities to do with additional staff
- Participant may try to “negotiate” with you
- Move past repetitive questions
- Consistent caregiver/staff members
Other Considerations

• No two PWS patients are the same
• Community engagement
  • Very well connected on social media and parent groups
  • Studies may have rules regarding social media
  • Community is dedicated
• Managing multiple studies
  • Maintain a participant prescreening log with key information
  • Set aside 30+ minutes for a new potential participant phone call

Questions?