United in Hope
FOR PWS

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NATIONAL CONVENTION

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Comprehensive Review of Digestive Issues in Prader-Willi Syndrome

Ann Scheimann MD MBA
Johns Hopkins School of Medicine
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Off-label Use Of Medications
Outline of Presentation

- Prevalence of gastrointestinal (GI) symptoms in Prader-Willi Syndrome
- Review of published clinical data, management approaches (evidenced-based and experiential in Prader-Willi syndrome)
  - Feeding/swallowing oral health
  - Gastric emptying/gastric dilation
  - Diarrhea
  - Constipation/rectal picking
How Common Are GI-related Symptoms?

- Early feeding difficulties very common among infants with PWS
  - Major criteria for clinical diagnosis of PWS (Holm, et al., Pediatrics 1993)

- Frequent reports of reflux symptoms, and inability to vomit
  - Early deaths from aspiration (Reflux related?)
  - Significant morbidity from high pain threshold and vomiting threshold well documented
Symptom Prevalence Among Adults With Prader-Willi Syndrome

Combined data from JV Butler et al. (2002), S Cassidy et al. (1995), and B. Whitman
FPWR Registry 2019: Frequency of Gastrointestinal Symptoms

- Reflux
- Rumination
- Gastroparesis
- Cholelithiasis
- Constipation
- Diarrhea
- Abdominal pain

Under 2 yrs, Over 2 years, Daily occurrence
Mortality in Children ≤ 5 years with Prader-Willi Syndrome: International Data

Cause of Death

- Aspiration
- Diarrhea
- Accidental
- Sepsis
- Pneumonia
- Obese/OSA
- Cardiomyopathy

Pooled published data from Europe, Australia, Japan, US
Mortality in Adults with Prader-Willi Syndrome: International Data

- Obese/pneumonia
- Accident
- Unknown
- Obese/OSA
- Stroke/PE
- Heart
- Aspiration
- GI

Pooled published data from Europe, Australia, Japan, US
Pediatric Deaths: PWSA USA Data

- Accident 9%
- Cancer 1%
- Cardiac 9%
- Choking 6%
- GI 6%
- GI perforation 3%

N=65

Courtesy of Jim and Carolyn Loker and PWSA | USA
Overview of GI Anatomy

Salivary gland

Esophagus

Stomach

Small Intestine

Large Intestine

Liver

Gallbladder

Pyloric valve

Pancreas

Ileocecal valve

Rectum

Anal sphincters
Common Oral Issues

- Oromotor weakness
  - Hypotonia
  - Palatal abnormalities

- Dental abnormalities
  - Micrognathia (Small jaw)
  - Microdontia (small teeth), delayed eruption and hypoplastic (weak) enamel, dental crowding and erosions from rumination

- Salivary abnormalities (xerostomia-thick saliva)
  - Salivary flow is only 20-50% of normals \((PS\text{ Hart, Ann NY Acad Sci 1998 and Saeves et al Arch Oral Biol 2012})\)
Phases of Swallowing

- Oral Preparatory
- Oral
- Pharyngeal
- Esophageal
Feeding and Swallowing interventions: Nutritional Intervention and Oromotor Therapy on NG Feeds in TCH Infants
Choking/Prader-Willi Syndrome

- Review of data provided by families and collected through the PWSA bereavement program
  - 39% of families reported history of choking among the 52 families who completed questionnaires
  - Choking listed as cause of death in 12/152 patients (7.9%)
  - Average age 24 years (3-52 years)
  - 92% of patients were male

Stevenson, Scheimann et al., AJMG 2008
Choking/Prader-Willi Syndrome

- Factors predisposing to choking
  - Hyperphagia/Foraging
    - 25% of patients were food-stealing
  - Thick saliva
  - Weakness of pharyngeal muscles
  - Gastritis/Gastroesophageal Reflux
    - Gastritis noted in 38% at autopsy (3/8)

Stevenson, Scheimann et al., AJMG 2008
Swallowing Issues Among Adults and Children with Prader-Willi Syndrome

• Study (2014) funded by PWSAUSA by Gross, Gisser and Cherpes
  • Findings published in Dysphagia 10/2015

• Swallow studies in adults with PWS seen in Pittsburgh

• VFSS Swallow Studies using thin liquids and barium cookies in 30 adults with PWS
  • Significant, sometime substantial pharyngeal residue was present in 97% of subjects
  • Moderate to severe esophageal stasis was detected in 100% of participants
  • None could feel pharyngeal residue or esophageal stasis, regardless of the quantity
Choking/Prader-Willi Syndrome

• Current Interventions
  • Heimlich maneuver training
  • Diet interventions
    • Supervised meals
    • Holiday monitoring
    • Meal pacing/Chewing prompts
    • Fluid intake with self regulation (straw)
  • Treatment of Gastritis/Gastroesophageal Reflux
Choking/Prader-Willi Syndrome

- Potential Interventions- III
  - Treatment of gastritis/reflux
    - Conservative measures
      - Watch meal volume
      - Elevate head of bed
      - Minimize caffeine
    - Decreased fat

- Potential Interventions-III
  - Treatment of gastritis/reflux
    - Antacids
      - Tums/Calcium
    - Acid suppression
      - H₂ Receptor
      - Proton pump inhibitor

? Screen for Helicobacter pylori in stool
### Bristol Stool Chart

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Separate hard lumps, like nuts (hard to pass)</td>
</tr>
<tr>
<td>Type 2</td>
<td>Sausage-shaped but lumpy</td>
</tr>
<tr>
<td>Type 3</td>
<td>Like a sausage but with cracks on the surface</td>
</tr>
<tr>
<td>Type 4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>Type 5</td>
<td>Soft blobs with clear-cut edges</td>
</tr>
<tr>
<td>Type 6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>Type 7</td>
<td>Watery, no solid pieces. Entirely Liquid</td>
</tr>
</tbody>
</table>
Anorectal Motility - Defecation

NASPghan motility teaching slide set

Image from http://msk-anatomy.com/
Frequency of Constipation in Prader-Willi Syndrome

- 21 patients with PWS (median age 32 with median BMI 23.6) at Aarhus Center
  - Constipation history, rectal exam, rectal diameter by ultrasound, transit time

- 30 healthy volunteers (median age 26 and BMI 23.1) controls

- Symptoms
  - Infrequent stools (<3/week) 47%
  - Straining 37%
  - Hard Stools 32%

- No difference in rectal diameter or transit time between PWS and controls
- 29.3% of PWS adults through questionnaire study

Kuhlmann et al, BMC Gastroenterology 2014; Equit Neurourology Urodynamics 2013
Constipating Conditions

- **Dysfunctional state**
  - Developmental (ADD, Cognitive)
  - Situational (Toilet/parent)
  - Psychogenic (Depression)
  - Constitutional (Genetic)
  - Reduced volume; drying

- **Metabolic/Endocrine**
  - Hypothyroid
  - Hypercalcemia
  - Lead
  - Diabetes mellitus
  - Hypopituitarism

- **Altered Anatomy**
  - Structural problem
    - (Position, Narrowing)
  - Acquired bowel stricture
  - Malrotation
  - Pelvic Mass
  - Aganglionosis (Hirschsprung’s)
  - Abnormal abdominal muscles (prune belly)
  - Abnormal nerves (Spina Bifida)
  - Hypotonia (CP/Myopathy)
  - Connective Tissue Disorder (Scleroderma, Lupus)
Treatment strategies for the preschool child

• For short duration stool withholding:
  • 1-2 initial cleansing enemas
  • Increase dietary fiber and softening agents
    • Milk of magnesia
    • Miralax
  • Goal is rectal emptying to allow gradual decrease in vault size with return of sensitivity
Toilet seating- Not this
Toilet seating- but this!
PWS GI Algorithm (Loker, Scheimann)

Management strategies for the school age child

• **Catharsis:**
  • Laxative- bisacodyl (5-10 mg) for 3-5 days or polyethylene glycol solution (Miralax/GoLytely)
  • Magnesium citrate

• **Maintenance**
  • Milk of Magnesia or Miralax
  • Toilet 5-10 minutes after meals with appropriate posture
  • Fiber rich diet plus water
Interventions for Constipation

Flaxseed
- Adjunct
- EFA
Coin lodged within the body of the stomach: from the Gastrolab Image Gallery
Treatment for Rectal Ulcer

- Relieve constipation and avoid straining during defecation
  - Consider stool softeners - titrate to keep stools soft
  - Decrease symptoms of pruritus ani from fecal bile acids

- Behavioral modification to decrease digging behavior
  - Supervised timed bathroom privileges
  - Reversed clothing to decrease anal access
  - Biofeedback/physical therapy to address toileting posture
Medical Alert on Constipation In Individuals with Prader-Willi Syndrome

- James Loker MD/CAB PWUSAUSA

“Failure of standard methods to clear stool in a timely manner in the setting of pain, distension, decreased appetite warrants surgical or GI consultation.”
Gastric Dilation
Gastric Dilation/Necrosis

- Severe acute gastric dilatation described by Simone-Emmanuel Duplay in 1883
- In dogs related to stretching then twisting of stomach along axis
- 1859 - Brinton suggested atony - inhibition of gastric motor nerves allowing progressive gastric distension
- Some models suggest feedback problem with solitary nucleus
Gastric Dilation/Necrosis

- Reported in anorexia and bulimia patients
  - Undernourished patients complain of abdominal pain after meals
  - Attributed to significant binge eating
  - Possible role of bacteria producing gas and wall injury
  - Gastric wall becomes thin; vascular compromise
  - In some cases accompanied by pancreatitis
  - Pancreatitis resulted from severe dilatation

- 17 yo with Rett Syndrome presented with history of abdominal distension, vomiting and constipation and breathholding-hypotensive/cyanotic at presentation
  - AXR with free Air with bloody ng lavage
  - Necrotic stomach at laparotomy with full thickness gastric necrosis
  - Etiology attributed to gastric atony and distension from air swallowing

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Gastric Dilation/Necrosis

- Difficult to diagnosis
- High index of suspicion
- Clinical features include change in diet before development of abdominal distension and vomiting
- Abdominal films show large dilated stomach
- Treatment is gastric decompression and supportive care with careful monitoring for possible rupture
Acute Gastric Dilatation with Gastric Necrosis in PWS

• Series of 6 women with vomiting and gastroenteritis developed rapidly progressive gastric dilatation followed by necrosis*
  • 2 Pediatric cases had spontaneous resolution
  • 1 patient died of sepsis
  • 3 patients had massive dilatation requiring gastrectomy in 2

• Another series of laparoscopic gastric banding reported one death in a patient with Prader-Willi Syndrome 45 days post procedure+

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+E Chelala et al., Surg Endo 1997, 268-71
Gastric Rupture/Necrosis: Recent Data

- 4 patients out of 152 died from gastric rupture/necrosis; 3 additional suspected
- Teen (BMI 22) binge eating on holiday followed by abdominal pain and vomiting
- 2 Young adults (not obese) with abdominal pain and vomiting
- Middle-aged obese adults with history of ulcer and gastritis
- Child with abdominal pain and hematemesis

Stevenson D, Scheimann A, et al., JPGN
Recent Case Report: Management of Recurrent Acute Gastric Dilatation in an Adult with PWS

- 36 yo male with PWS, BMI 30, controlled dietary intake in group home

- ER presentation with abdominal pain and vomiting after binge eating- CT with dilated stomach and free air- diagnostic laparoscopy negative. Treated with abx and ng tube HD 9

- 7 months later- abd pain, vomiting, resp distress after binge eating with acute gastric dilation and aspiration pneumonia- significant NG output. Had cardiac arrest and PE but survived
  - Subsequent EGD with residual food in stomach regurgitating to esophagus despite trials of neostigmine and metoclopramide
  - Had PEG placed with jtube extension to allow gastric venting and jejunal feedings (patient refused NG tube)

Mohammed AM and Dennis RJ. J Surg Case Rep 2016
Diet Strategies for Gastroparesis

- Small frequent meals
- Watch fiber intake
- Prioritize protein in the diet
- Increase fluid in foods
- Chew foods well since stomach may not grind effectively
- Remain upright and move to help move food along
Final Thoughts

“The world is full of challenges, but with those come opportunity, and I am an opportunist.”

Acknowledgements

- Collaborators
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THANK YOU

www.pwsausa.org

Info@pwsausa.org

(941) 312-0400