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New Era of Adult Gut Rehabilitation and Transplantation-Medical/Surgical Management of GLP-2 Analog in the Clinical Space

Disclosures
- I have no commercial relationships to disclose

Presentation Overview/Summary
GLP-2 analog is a novel therapy that has been proven to enhance remnant gut adaptation. Its therapeutic goal is to accelerate a patient’s adaptation, wean PS and to improve quality of life. The use or initiation of GLP-2 takes careful thought and assessment. Patients on GLP-2 therapy require diligent monitoring to achieve positive response. GLP-2 related symptoms may be troubleshooted and often do not require discontinuation of GLP-2 therapy. If unable to achieve a positive response, lack of response to therapy should be evaluated and triage to surgery should be considered.

Learning Objectives
At the conclusion of the presentation, the learner will be able to:
1. Recognize qualifications for use of GLP-2 analog in clinical practice
2. Summarize parenteral support (PS) weaning strategies with the use of GLP-2 analog
3. Understand clinical observations and experiences to better troubleshoot symptoms of GLP-2 analog

Key Takeaways/Fast Facts
- GLP-2 Analog can be utilized in a wide array of SBS population with varying anatomy, disease state and varying degree on reliance of PS.
- Diligent monitoring in patients for GLP-2 response is essential for positive outcomes and PS weaning.
- GLP-2 Analog related symptoms may be troubleshooted and often do not require discontinuation of GLP-2 therapy.
- Lack of response to therapy should be evaluated. If unable to achieve a positive response, triage to surgery should be considered.

Learning Assessment Questions
1. Which of the following are insurance qualifiers for the use of GLP-2 analog?
   A. SBS and dependence on PN
   B. SBS and dependence on PS
   C. IBD and dependence on PS
   D. IBD and dependence on PN

2. Which of the following clinicals are essential in monitoring a patient on GLP-2 analog?
   A. Laboratory assessments of electrolytes and hydration
   B. Weight
   C. Intake and output
   D. All of the Above

Learning Assessment Answers:
1. Answer = B; Rationale: The FDA and insurance companies require the patient to have a short bowel syndrome diagnosis and need to be dependent on some kind of intravenous support (this is non-specific and does not require a patient be on parenteral nutrition).
2. Answer = D; Rationale: Careful monitoring of patients on GLP-2 analog requires assessment of labs that assess hydration and electrolytes, weight to rule out excessive wt gain or loss (possibly due to fluid overload and/or improved absorption of fluids and/or macronutrients) and intake and output records to determine if patient is in positive or negative fluid balance. These monitoring clinicals will help a provider determine if a patient is appropriate to undergo PS weaning and to what extent a formulation should be weaned.

References


Medical/Surgical Management of GLP-2 Analog in the Clinical Space

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Learning Objectives

1. Recognize qualifications for use of GLP-2 analog in clinical practice
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GLP-2 Analog Clinical Trials

**Phase II**
- Open label, non-placebo controlled, 21 day
- Metabolic Studies and Mucosal Biopsy
- ↑ wet weight absorption
- ↑ villus height
- ↑ villus crypt depth
- ↑ Miotic Index
- *all effects returned to baseline 3 weeks post therapy*

**Phase III**
- Randomized, double blind, placebo controlled, 24 week multi-center study
- ↑ responder rate
- ↑ reduction in PS volume from baseline
- ↑ % response per visit
- ↑ plasma citrulline
- ↓ Subject weight gain

**Phase III Study Extension**
- Randomized, double blind, placebo controlled, 28 week extension study
- ↓ PS volume (52% with 0.05 mg/kg dosage; 26% with 0.1 mg/kg dosage)
- ↑ responder rate after 52 weeks (both groups)
- ↑ plasma citrulline
- 4 subjects weaned from PS completely
- 52% reported GLP-2 related Adverse Event (GI disturbance)

Initiation of GLP-2 Analog: Indications for Use

**INSURANCE QUALIFIERS**
- Short Bowel Syndrome (ICD 10 Codes: K91.2, K90.9)
- Dependence on Parenteral Support (PS)

**PRACTICAL CLINICAL QUALIFIERS**
- Very reduced length of small bowel & PS dependence is indefinite
- Adequate length of small bowel & on standard SBS therapy, but no progression
- Status post lengthening or reconstructive surgery & unable to achieve PS wean
- Frequent dehydration or frequent kidney stones
- Dependence on intravenous fluids (IV) and/or IV electrolytes
- Require minimal PS on standard SBS therapy

Initiation of GLP-2 Analog: Special Considerations

- Active cancer dx or history (polyps in colon or rectum)
- Gallbladder, Pancreas, or kidney issues
- Obstructive Disease
- Congestive Heart Failure (CHF) dx
- Pregnant or lactating
- Activity of Inflammatory Bowel Disease (IBD)
- Non-compliance
- Recent GI surgery
- Other medication absorption
- Ability to tolerate PO/enterals
Monitoring for Clinical Response

Initial Phase
- Biweekly assessment
- Laboratory Measures of electrolytes and hydration
- Intake and Output, weight and clinical symptoms
- Adjustment of PS dependent on urine output and clinical judgement
- Continue biweekly assessment (or more frequent) until PS adjustment is null

Maintenance Phase
- Monthly assessment
- Laboratory Measures of electrolytes and hydration
- Intake and Output, weight and clinical symptoms
- Adjustment of volume based on urine output and clinical judgement
- Once a patient reaches a PS frequency of 3 days per week; may consider attempting discontinuation

Seidner et al. JPEN. 2013;37(2):201-211.

Weaning PS on GLP-2 Analog

PRACTICAL WEANING

URINE OUTPUT BASED WEANING

<table>
<thead>
<tr>
<th>Urine Output</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 liter/day</td>
<td>Increase PS volume to previous volume</td>
</tr>
<tr>
<td>&gt;1 liter/day and &lt; baseline urine</td>
<td>Increase or maintain PS volume</td>
</tr>
<tr>
<td>≥ baseline urine and &lt;10% increase over baseline urine</td>
<td>Maintain current PS volume</td>
</tr>
<tr>
<td>&gt; baseline urine and up to 2 liters/day</td>
<td>Decrease PS volume by 10% based on clinical judgement</td>
</tr>
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<td>&gt; 2 liters/day</td>
<td>Decrease PS volume by &gt;10% based on clinical judgement</td>
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GLP-2 Analog Symptom Management

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<td>Antiemetic</td>
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<td>Assess for SBS</td>
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<tr>
<td>Partial Bowel Obstruction</td>
<td>Adjust antidiarrheals</td>
</tr>
<tr>
<td>Elevate Enzymes</td>
<td>Check imaging</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>Examine weight gain</td>
</tr>
<tr>
<td>Edema/Sudden weight gain</td>
<td>Adjust PS volume</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Adjust PS or oral electrolytes</td>
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Weaning PS on GLP-2 Analog

Management of GLP-2 Analog in the Clinical Space

Recap
- Indications for GLP-2 Analog use are not concrete, but qualify a wide array of SBS patients
- Diligent monitoring of GLP-2 Analog is imperative in achieving PS weaning success and noting positive clinical response
- GLP-2 Analog related symptoms may be troubleshooting and often do not require discontinuation of GLP-2 therapy
- Lack of response to therapy should be evaluated. If unable to achieve a positive response, triage to surgery should be considered

References

New Era of Gut Rehabilitation and Transplantation
Part 1 Talk: Succinct Overview of Gut Rehabilitation and Adaptation.

Disclosures
- “I have no commercial relationships to disclose”

Presentation Overview/Summary
- A number of therapeutic options exist for the management of SBS with the goal of minimizing complications, such as dehydration, malnutrition, and parenteral support (PS) complications, and minimize morbidity and mortality. Spontaneous changes in the remnant bowel typically happen within 2-5 years after resection leading to more efficient absorption. The success of adaptation with weaning of PS is based on the length and anatomical configuration of the remaining bowel. Patients may need more aggressive treatment options to help promote adaptation and PN weaning such as GLP-2 analog or surgical reconstruction.

Learning Objectives
At the conclusion of the presentation, the learner will be able to:
1. Summarize the goals of gut rehabilitation
2. Differentiate the potential for parenteral support (PS) independence in each classification of Short Bowel Syndrome
3. Identify factors that promote intestinal adaptation

Key Takeaways/Fast Facts
- Our main goals of managing patients with short bowel syndrome (SBS) are to maintain hydration/nutrition while trying to minimize PS use, manage complications-particularly PS complications and minimize morbidity and mortality.
- Adaptation usually happens within the first 2-5 years after bowel resection.
- The success with weaning of PN is based on the length and anatomical configuration of the remaining bowel.
- Patients may need more aggressive treatment options to help promote adaptation and PN weaning such as GLP-2 analog or surgical reconstruction.

Learning Assessment Questions
1. Which type of short bowel syndrome is least likely to need parenteral support
   A. 75 cm of jejunum to and end jejunostomy
   B. 50 cm of jejunum to an jejuno-colonic anastomosis
   C. 50 cm of jejunum anastomosed to 110cm of ileum with ileocal valve and intact colon.

Learning Assessment Answers:
1. Answer = C; Rationale: patients with a jejuno-ileal anastomosis, ileo-cecal valve, and intact colon in continuity rarely require PS -- Ileum shows greater adaptation response over the
The presence of colon lends ability to absorb water, electrolytes, and fatty acids, produced from the fermentation of undigested carbohydrates by colonic bacteria; slow intestinal transit; and stimulates intestinal adaptation.

References

New Era of Adult Gut Rehabilitation and Transplantation

Lisa Moccia RD, LD, CNSC (moderator)
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Kishore Iyer, MD, FRCS

A Succinct Overview of Gut Rehabilitation and Adaptation

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Learning Objectives

1. Summarize the goals of gut rehabilitation
2. Differentiate the potential for parenteral support (PS) independence in each classification of Short Bowel Syndrome
3. Identify factors that promote intestinal adaptation

Goals of Gut Rehabilitation

- Maintain fluid, electrolyte and nutritional status
- Minimize PS dependency
- Prevent PS complications
- Minimize morbidity and mortality

Brief Overview of Gut Adaptation

Adaptation: Spontaneous changes that lead to more efficient absorption per unit length of small bowel
- Duration:
  - Two years post intestinal insult
  - Up to 4-5 years with Gut Rehab Program support
- Adaptation outcome post intestinal resection:
  - 1 year: 74% dependence on PS
  - 5 years: 48% dependence on PS

The Remnant Bowel and Adaptation

- TYPE I SHORT BOWEL: end jejunostomy (SBS-J)
- TYPE II SHORT BOWEL: jejuno-colic anastomosis (SBS-JC), remnant jejunum in continuity with a portion of the colon (often left colon)
- TYPE III SHORT BOWEL: jejuno-ileal anastomosis (SBS-JI) with ileocecal valve and intact colon in continuity

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Bowel Length and PN Weaning

Factors and Therapies that Influence Adaptation

Factors that Influence Adaptation
- Enteral nutrition
- Whole foods (hyperphagia)
- Endogenous Trophic Hormones

Therapies that Promote Adaptation

Treatment of overgrowth
- Trophic hormones
- GLP-2 analog

Surgical interventions
- Bowel lengthening
- Bowel reconstructive surgery
- Gut and intestinal transplant

References
3. Tappenden KA. Intestinal adaptation following resection. JPEN. 2014;38(S1):23s-31s.