ASPEN EDUCATION PROGRAM OUTLINE TEMPLATE

Cassandra Pogatschnik RD, LD, CNSC, Advanced Practice I Clinician, Center for Gut Rehabilitation and Transplantation and Center for Human Nutrition, Cleveland Clinic

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

1. Jeppesen PB, Sanguinetti EL, Buchman A, Howard L, Scolapio JS, Ziegler TR, Gregory J, Tappenden, Holst J, Mortensen PB. Teduglutide (ALX-0600), a dipeptidyl peptidase IV resistant glucagon-like peptide 2 anaologue, improves intestinal function in short bowel syndrome patients. Gut 2005;54: 1224-1231.
2. Jeppesen PB, Gilroy R, Pertkiewicz M, Allard JP, Messing B, O'Keefe SJ. Randomized placebo-controlled trial of teduglutide in reducing parenteral nutrition and/or intravenous fluid requirements in patients with short bowel syndrome. Gut 2011;60:902-914.
3. Vipperla K, O'Keefe J. Study of teduglutide effectiveness in parenteral nutrition-dependent short-bowel syndrome subjects. Gastroenterol. Hepatol. 2013;7(8):683-687.
4. Seidner DL, Schwartz LK, Winkler MF, Jeejeebhoy K, Boullata JI, Tappenden KA. Increased intestinal absorption in the era of teduglutide and its impact on management strategies in patients with short bowel syndrome-associated intestinal failure. JPEN. 2013;37(2):201-211.

ASPEN 2019 Nutrition Science & Practice Conference

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

Cassandra Pogatschnik RD, LD, CNSC
Advanced Practice I Dietitian
Center for Gut Rehabilitation and Transplantation and Center for Human Nutrition
Cleveland Clinic, Cleveland, OH

Disclosures

- I have no commercial relationships to disclose

Learning Objectives

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

GLP-2 Analog Clinical Trials

Clinical Trial	Study Design	Result with GLP-2 Analog
Phase II	Open label, non-placebo controlled, 21 day Metabolic Studies and Mucosal Bx	↑ 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	↑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 0.1mg/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) Discontinuation of drug led to ↑ PS volume

Jeppesen P, et al. Gut 2005;54:1224-1231.
Jeppesen P, et al. Gut 2011;60:902-914.
Vipperla K, et al. Gastroenterol Hepatol. 2013;7(8):683-687.

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
- Frequently 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 of lactating
- 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 with each set of labs
- 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**

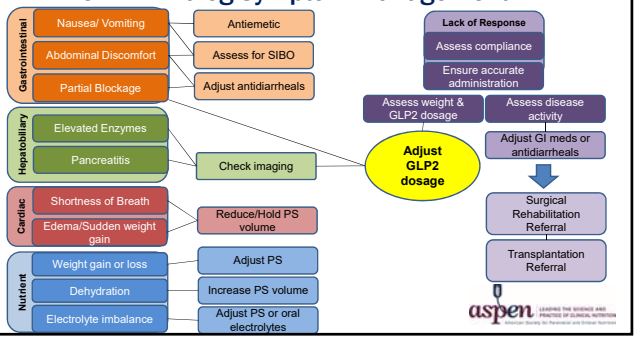
Seidner et al. JPEN. 2013;37(2):201-211.

Weaning PS on GLP-2 Analog

PRACTICAL WEANING	URINE OUTPUT BASED WEANING
PS reduction per clinical judgement if: • Weight gain • Symptoms of overhydration • Increased urine output • Significantly reduced feculent losses • Lab work reflects dilution	**If urine output is:** • < 1 liter/day → increase PS volume to previous volume • >1 liter/day and is < baseline urine →increase or maintain PS volume • ≥ baseline urine and <10% increase over baseline urine → maintain current PS volume • ≥ increase over baseline urine and up to 2 liter/day → decrease PS volume by 10% • ≥ increase over baseline urine and > 2 liters/day → decrease PS volume by >10% ~~based on clinical judgement~~

Jeppesen P, et al. Gut 2011;60:902-914.

GLP-2 Analog Symptom Management



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 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 PS

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

References

1. Jeppesen PB, Sanguinetti EL, Buchman A, Howard L, Scolapio JS, Ziegler TR, Gregory J, Tappenden, Holst J, Mortensen PB. Teduglutide (ALX-0600), a dipeptidyl peptidase IV resistant glucagon-like peptide 2 anaologue, improves intestinal function in short bowel syndrome patients. Gut 2005;54: 1224-1231.
2. Jeppesen PB, Gilroy R, Pertkiewicz M, Allard JP, Messing B, O'Keefe SJ. Randomized placebo-controlled trial of teduglutide in reducing parenteral nutrition and/or intravenous fluid requirements in patients with short bowel syndrome. Gut 2011;60:902-914.
3. Vipperla K, O'Keefe J. Study of teduglutide effectiveness in parenteral nutrition-dependent short-bowel syndrome subjects. Gastroenterol. Hepatol. 2013;7(8):683-687.
4. Seidner DL, Schwartz LK, Winkler MF, Jeejeebhoy K, Boullata JI, Tappenden KA. Increased intestinal absorption in the era of teduglutide and its impact on management strategies in patients with short bowel syndrome-associated intestinal failure. JPEN. 2013;37(2):201-211.

ASPEN EDUCATION PROGRAM OUTLINE TEMPLATE

Lisa Moccia RD LD CNSC
Advanced Practice 1 Clinical Dietitian
Center for Gut Rehabilitation & Transplantation/ Center for Human Nutrition
Cleveland Clinic

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

jejunum. 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

1. Amiot A. Messing B, Corocos O, Panis Y, Joly F. Determinants of home parenteral nutrition dependence and survival of 268 patients with non-malignant short bowel syndrome. Clinical Nutrition 32 (2013) 368-374.
2. Messing B, Crenn P, Beau P, Boutron-Ruault M, Rambaud JC, Matuchansky C. Long-term survival and parenteral nutrition dependence in adult patients with the short bowel syndrome. Gastroenterol. 1999;117:1043-1050.
3. Tappenden KA. Intestinal adaptation following resection. JPEN. 2014;39(S1):23s-31s.

ASPEN 2019 Nutrition Science & Practice Conference

New Era of Adult Gut Rehabilitation and Transplantation

Lisa Moccia RD, LD, CNSC (moderator)
Douglas Burrin PhD
Cassandra Pogatschnik RD, LD, CNSC
Kishore Iyer, MD, FRCS

ASPEN 2019 Nutrition Science & Practice Conference

A Succinct Overview of Gut Rehabilitation and Adaptation

Lisa Moccia RD, LD, CNSC
Advanced Practice I Dietitian
Center for Gut Rehabilitation and Transplantation and Center for Human Nutrition
Cleveland Clinic, Cleveland, OH

I have no commercial relationships to disclose

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

⇩

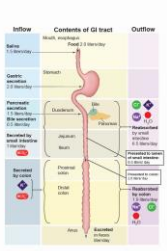
Minimize PS dependency

⇩

Prevent PS complications

⇩

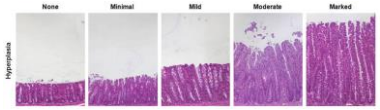
Minimize morbidity and mortality



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



Amiot et al. Clin Nutr. 2013; 32:368-374.

The Remnant Bowel and Adaptation

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

Bowel Length and PN Weaning

GASTROENTEROLOGY 1999;117:1043–1050

ALIMENTARY TRACT

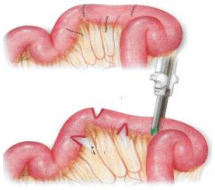
Long-term Survival and Parenteral Nutrition Dependence in Adult Patients With the Short Bowel Syndrome

BERNARD MESSING,* PASCAL CRENN,* PHILIPPE BEAU,† MARIE CHRISTINE BOUTRON–RUAULT,* JEAN–CLAUDE RAMBAUD,* and CLAUDE MATUCHANSKY*
*Department of Hepatogastroenterology and Nutrition Support and INSERM Unité 290, Hôpital Lariboisière-Saint-Lazare, Paris; and †Department of Hepatogastroenterology and Nutrition Support, Hôpital La Milétrie, Poitiers, France

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



Tappenden KA. JPEN 2014;38:23S-31S.

References

1. Amiot A. Messing B, Corocos O, Panis Y, Joly F. Determinants of home parenteral nutrition dependence and survival of 268 patients with non-malignant short bowel syndrome. Clinical Nutrition 32 (2013) 368-374.
2. Messing B, Crenn P, Beau P, Boutron-Ruault M, Rambaud JC, Matuchansky C. Long-term survival and parenteral nutrition dependence in adult patients with the short bowel syndrome. Gastroenterol. 1999;117:1043-1050.
3. Tappenden KA. Intestinal adaptation following resection. JPEN. 2014;39(S1):23s-31s