3 yo boy with congenital anomalies and hypoglycemia

Endorama

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HPI

- 35 mo Caucasian boy w/ complex medical history, GH def & h/o hypoglycemia presents w/ episodes of hyper- and hypoglycemia
- 30 min. postprandially mom noticed "lethargy" → BG 352 mg/dL
- 1 hr PP → BG 267 mg/dL
- 3.5 hrs PP → BG 40 mg/dL at PMD
- BG 156 in the Comer ED
- Admitted for evaluation and management

ROS

- Dx with SOD and GH def. at age 12 mo following episode of hypoglycemia
- Treatment with Nutropin 0.3mg/kg/week
- Baseline: BG nadir 50-60 mg/dL once q1-2 mo
- Past 2 months:
  - ↑ mid-afternoon episodes (BG 30-50) with 2 episodes of BG > 200
  - ↑ episodes of "lethargy"
  - Multiple URIs w/ O2 requirement, recently weaned
  - Changed from po ad lib diet to strict feeding schedule: Neocate 8 oz TID thickened + po diced/chopped food
- Poor weight gain and poor appetite
- Stable, chronic diarrhea
- Baseline abdom distention slightly increased

PMH

Problem List

- Chromosome 17 inversion
- Septo-optic dysplasia
- GH deficiency
- Tricuspid atresia/ASD/VSD
- Portal vein thrombosis w/ extrahepatic portal HTN
- Esophageal varices
- FTT
- h/o dysphagia
- Right eye visual impairment
- Bilateral hearing impairment
- Recurrent otitis media
- Steatorrhea
- Global developmental delay

PSH

- 2 mo: B-T shunt
- 4 mo: Glenn procedure
- 12-18 mo: cauterization of varices followed by Sugiura procedure
- ~15 mo: G-tube & Nissen fundoplication

History cont'd

Birth Hx

- Full-term c-section
- Postnatal resp distress→CHD
- Dysmorphic features

Medications

- Lasix
- Prevacid
- Nutropin AQ 0.3mg/kg/wk
- Probiotic
- Augmentin for recent AOM

Family History

- Mother: prematurity, Tetralogy of Fallot, obesity
- Father: sleep apnea, obesity
- Healthy 4 yo brother
- No diabetes, other congenital anomalies

Physical Exam

T 37.4 C HR 124 RR 40 BP 125/72 O2Sat 85%

Lt: 83.7cm (- 3 SD), wt: 12 kg (5th%), Wt-for-Lt: 60th%, HC 49.6 cm (48th%)

Gen: small, thin

HEENT: prominent forehead, hypoplastic L pinna, low set ears, hypertelorism, small, thin lips, anteverted nose, no thyromegaly

CV: 3/6 SEM, RRR, 2+ pp, sl. cyanosis of lips and nail beds, mid-sternal scar

Lungs: CTAB, no wheezes, + loud upper airway noise

GI: markedly distended with prominent superficial veins, L transverse scar, + G-tube, + splenomegaly

GU: Stretched penile lt 4.3 cm, testes descended bilat, large bilat inguinal hernias

MSK: no muscle atrophy, + digital clubbing

Neuro: unable to elicit DTRs, normal tone and gait

Skin: pale, nl pigment

Differential Diagnosis?

In a 3 yo w/

- postprandial hyper- and hypoglycemia
- SOD w/ GH def, FTT, chronic diarrhea
- s/p cardiac and GI surgery

- Dumping syndrome
- Impending type 2 DM, insulin autoantibodies (rarely presents this way in children)
- Glycogen synthetase def. (less likely)

Initial labs

1 week prior, non-fasting @ 1:10pm

- Serum glucose 145 mg/dL, nl lytes
- Cortisol 6.3 mcg/dL ACTH 11.1 pg/mL
- nl TFTs

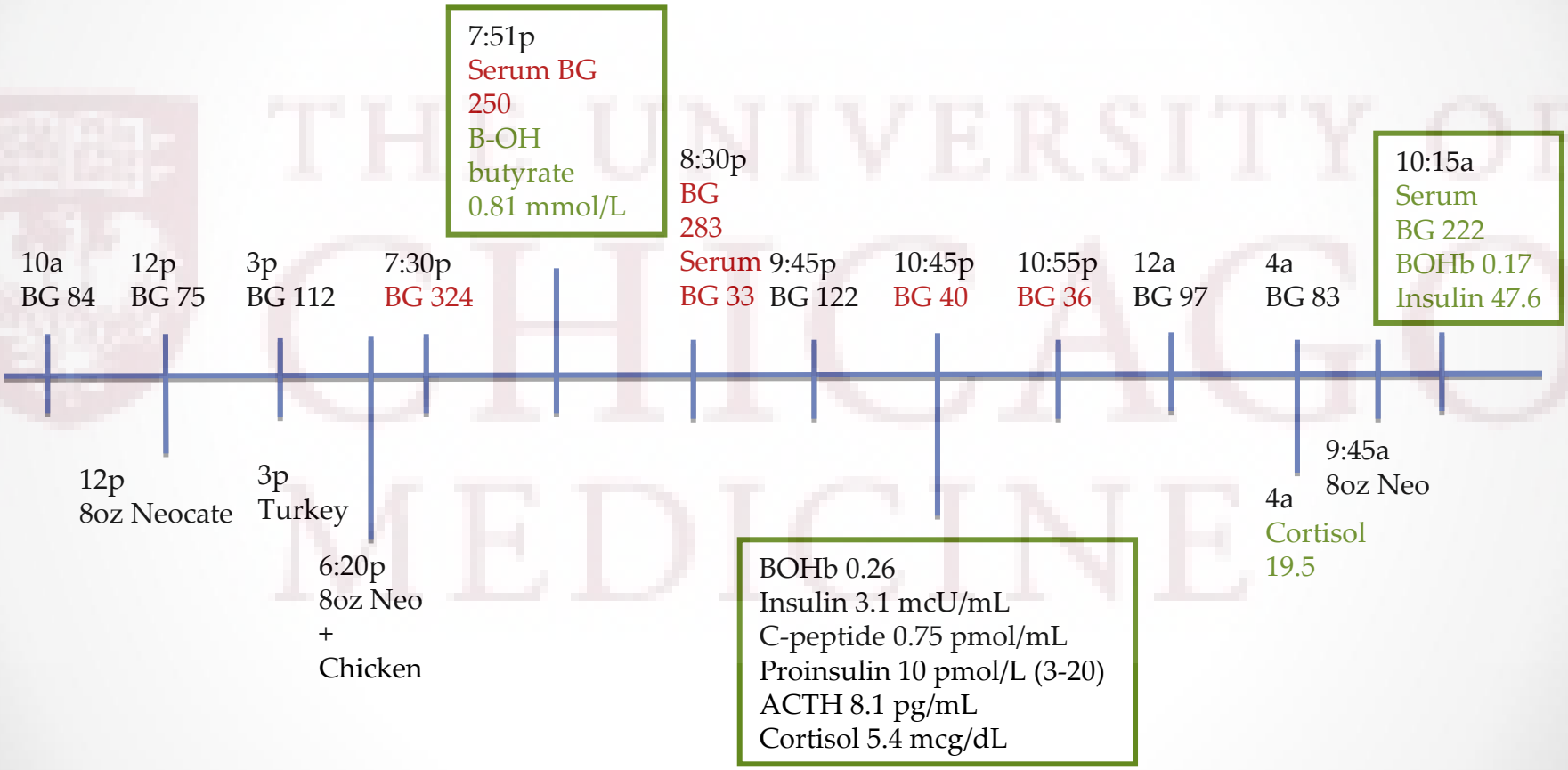
Upon admission

- Serum glu 145 C-peptide 3.26 pmol/mL(0.3-2.35)
- HbA1c 5.8% GAD65/IA2/Insulin ab neg

Planned OGTT

BG > 60 during12 hr overnight fast

Evaluation


7:51p
Serum BG
250
B-OH
butyrate
0.81 mmol/L
8:30p
BG
283
10:15a
Serum
BG 222
BOHb 0.17
Insulin 47.6
10a
BG 84
12p
BG 75
3p
BG 112
7:30p
BG 324
Serum
BG 33
9:45p
BG 122
10:45p
BG 40
10:55p
BG 36
12a
BG 97
4a
BG 83
12p
8oz Neocate
3p
Turkey
6:20p
8oz Neo
+
Chicken
BOHb 0.26
Insulin 3.1 mcU/mL
C-peptide 0.75 pmol/mL
Proinsulin 10 pmol/L (3-20)
ACTH 8.1 pg/mL
Cortisol 5.4 mcg/dL
4a
Cortisol
19.5
9:45a
8oz Neo

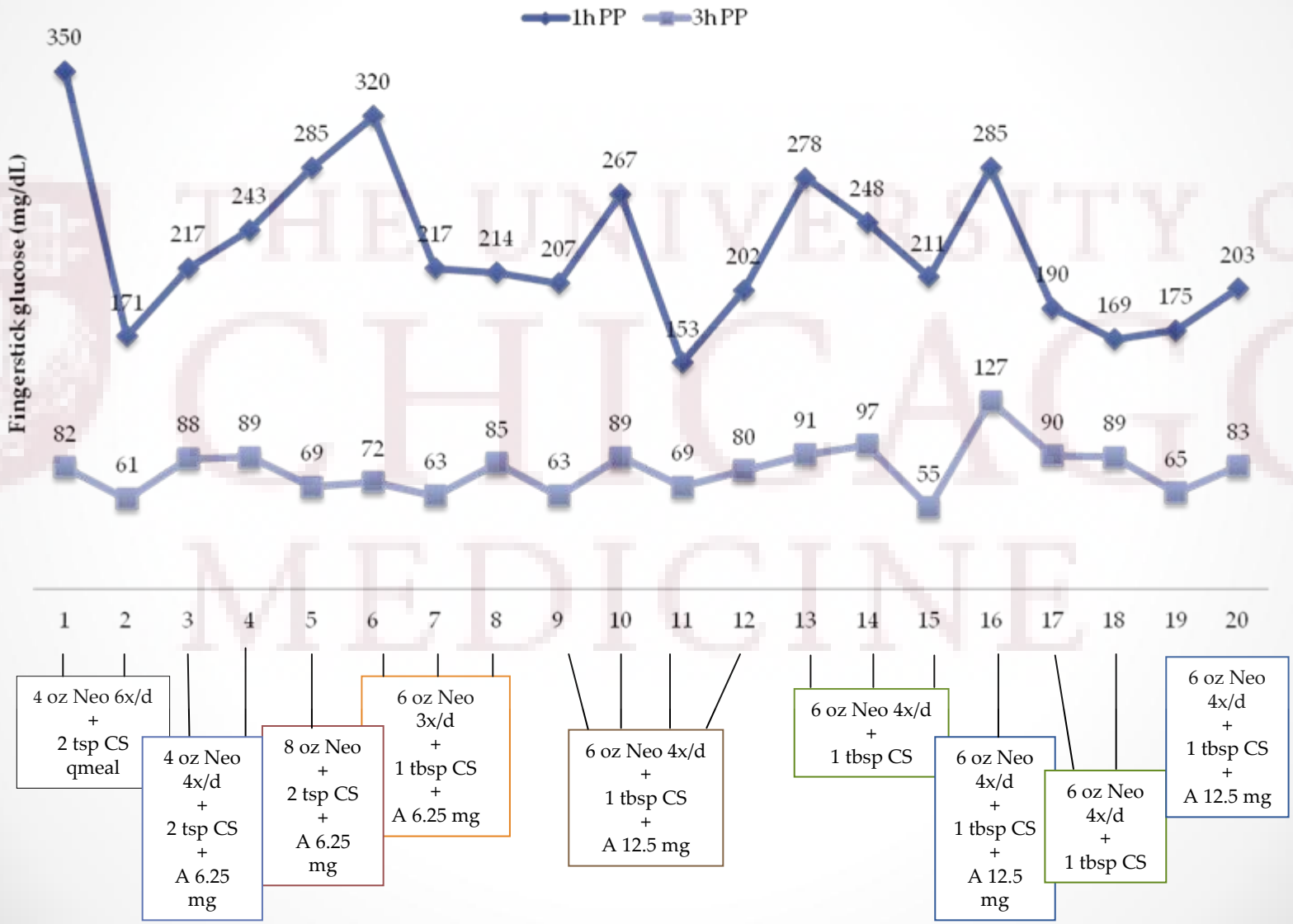
Diagnosis

- Postprandial hyperglycemia with mild ketosis followed by hypoglycemia with inappropriately elevated insulin level:

Dumping Syndrome

- In children, most frequently occurs post-fundoplication, especially with pyloroplasty
- Sx: refusal to eat, lethargy, nausea, tachycardia, diaphoresis, watery diarrhea
- Early: within 30-60 min post-prandially
- Late: within 90-240 min post-prandially[1]

Glucose Pattern

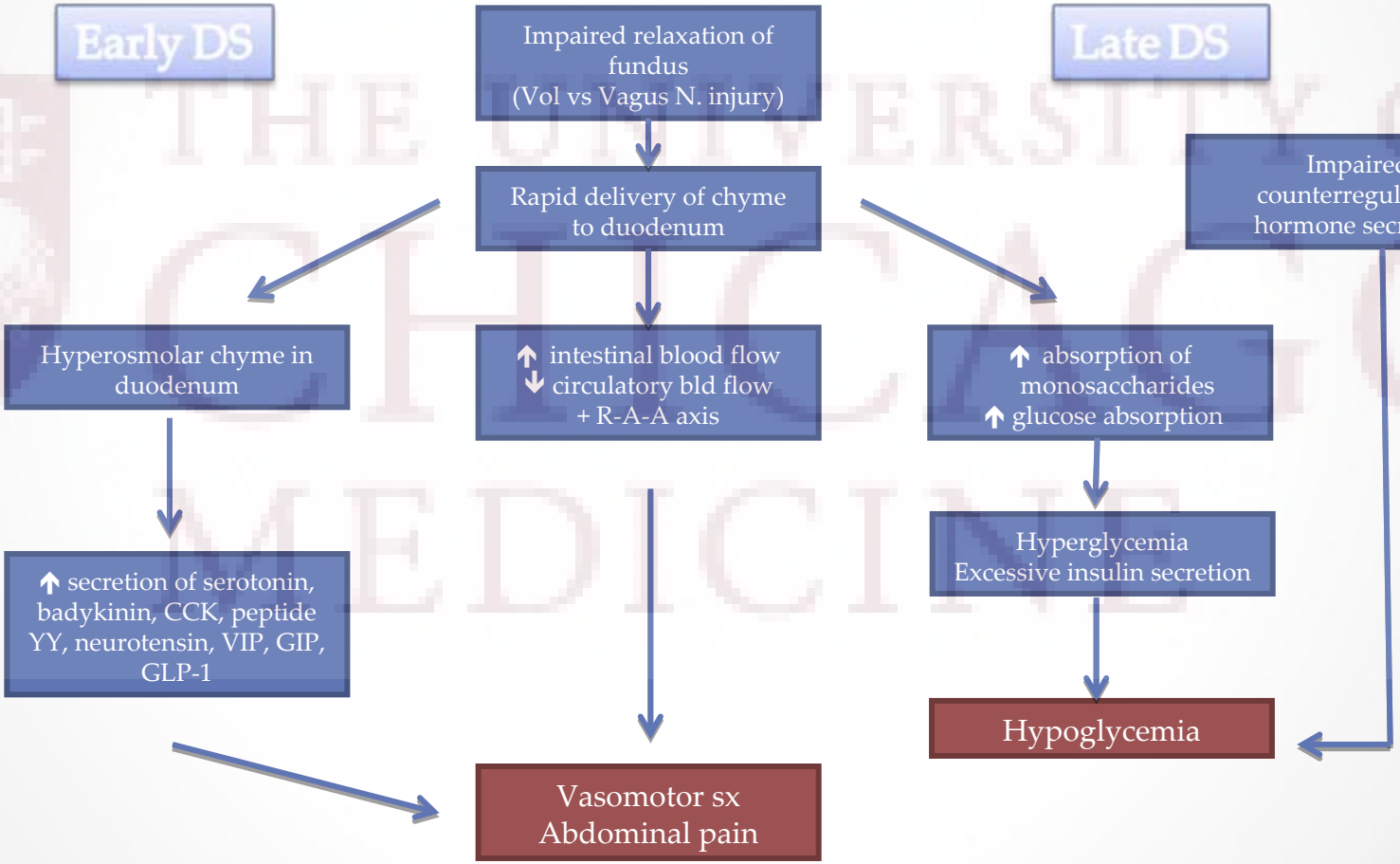


- Neo=Neocate, CS=cornstarch, A= Acarbose

Clinical Questions

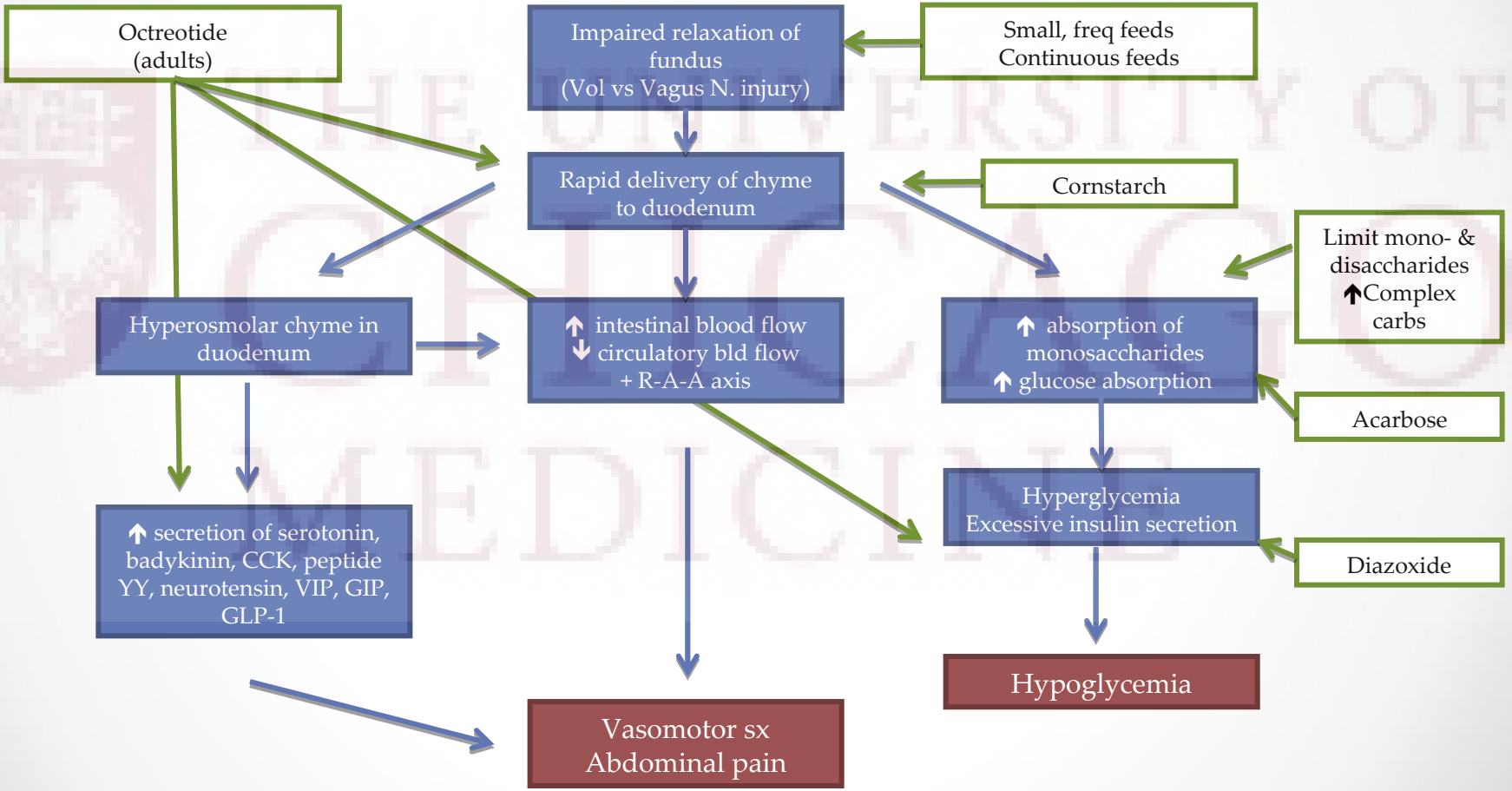
- Pathogenesis of dumping syndrome following Nissen fundoplication?
- Current treatment strategies for pediatric disease?
- Acarbose: safe and efficacious in children?

Pathogenesis



Butler P, et al. *Pediatr Surg Int*, 2001
Tack J, et al. *Nat Rev Gastroenterol Hepatol* 2009

Treatment



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Tack J, et al. *Nat Rev Gastroenterol Hepatol* 2009
Khoshoo et al. *Arch Dis Child* 1991

Acarbose treatment in children

- Acarbose
  - a-Glucosidase inhibitor
  - Delays oligosaccharide → monosaccharide conversion
- May be well tolerated and effective, data limited
  - Ng et al: 6 pts s/p Nissen fundoplication and severe, symptomatic hypoglycemia (mean nadir of 33 ± 2 mg/dL) at 120-140 min post-prandially
    - All responded to Acarbose prior to each bolus feed: 12.5 up to 50 mg
    - Adverse effects: flatulence
  - Cunto et al: 8 pts s/p Nissen with confirmed post-prandial hypoglycemia
    - 4/8 received high-dose Acarbose w/ each feed: 30-100mg
    - No adverse effects
    - Surveillance period unknown

Conclusion

- Suspect dumping syndrome in children with insulin dysregulation with a history of gastric surgery
- Dumping syndrome is caused by increased gastric motility resulting in hormonal dsyregulation
- Acarbose may be a safe and effective adjunct to dietary modifications and cornstarch, though more long-term studies are needed

References

1. Butler P, Ehringhaus, Koletzko. Dumping syndrome: a common problem following Nissen fundoplication in young children. *Pediatr Surg Int* 2001; 17: 351-55.
2. Tack J, Arts J, Caenepeel P, DeWulf D, Bisschops R. Pathophysiology, diagnosis and management of postoperative dumping syndrome. *Nat Rev Gastroenterol Hepatol* 2009; 6: 583-90.
3. Khoshoo V, Reifen RM, Gold BD, Sherman PM, Pencharz PB. Nutritional manipulation in the management of dumping syndrome. *Arch Dis Child* 1991; 66(12): 1447-8.
4. Ng, DD, Ferry RJ, Kelly A, Weinzimer SA, Stanley, CA, Katz, LEL. Acarbose treatment of hypoglycemia in children after Nissen fundoplication. *J Pediatr* 2001; 139; 877-9.
5. Cunto AD, Egidio B, Minen F, Ventura A. Safety and efficacy of high-dose acarbose treatment for dumping syndrome. *J Pediatr Gastroenterol Nutr* 2011; 53: 113-14.