Low Dose Glucagon for Non-Emergent Hypoglycemia at Diabetes Camp

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Hypoglycemia with Type 1 Diabetes

- Hypoglycemia is a common complication of insulin therapy
- Rates of coma and convulsions estimated to be 20 events/100 patient years in children on conventional therapy
- Insulin analogs and pump therapy may improve these rates

Jones et al. Pediatric Diabetes 2003:4:143-150

Hypoglycemia with Type 1 Diabetes

- Use of glucose sensor technology has shown widespread occurrence of asymptomatic hypoglycemia
- Hypoglycemia unawareness is common and increases the risk of severe low BG
- Whether episodes have long term consequences is controversial

Jones et al. Pediatric Diabetes 2003:4:143-150

Hypoglycemia at Camp

- However – hypoglycemia definitely interferes with camp activities!
- Hypoglycemia may be more common at camp than at home due to:
  - Altitude
  - Increased activity
  - Lower fat diet at camp

Glucagon Treatment for Hypoglycemia

- Glucagon raises BG levels by converting liver glycogen to glucose which is released into the circulation
  - ½ life is 8-18 minutes
  - Maximum plasma concentrations occur 13 to 18 min after IM and 20 min after SQ
  - Peak after 1 mg occurs 26-30 min after IM and SQ injection

Pearson. The Diabetes Educator 2008:34:128-134

Mini-Dose Glucagon (GCG)

- Two articles describing Mini-Dose GCG
  - Haymond and Schreiner. Mini-Dose Glucagon Rescue for Hypoglycemia in Children With Type 1 Diabetes

    Diab Care 2001:24:643-645
  - Hartley, Thomsett and Cotterill. Mini-Dose Glucagon Rescue for Mild Hypoglycaemia in Children with Type 1 Diabetes: The Brisbane Experience. J Paed Child Health 2006:42:108-111

Mini-Dose Glucagon

- Haymond and Schreiner
  - Hypoglycemia BG <5.5 mmole/l (99 mg/dl) and sick
  - 33 episodes in 28 children ages 6.6+/- 0.7 yrs
  - Dose: 10 mcg/year of age up to 150 mcg
  - BG before GCG: 3.44+/- 0.15 mmole/l (62+/-2.7 mg/dl)
  - BG after GCG: 8.11 +/- 0.72 mmole/l (146 +/-13 mg/dl)
  - Glucagon was well tolerated

Diab Care 2001:24:643-645

Mini-Dose Glucagon

- Brisbane Experience
  - Hypoglycemia BG <4 mmole/l (72 mg/dl)
  - Associated with inability to eat or food refusal
  - 38 episodes in 25 children age <12 years
  - Dose: 10 mcg/year of age up to 150 mcg
  - Child managed at home on 32 (84%) and 6 (16%) required hospitalization
  - Additional doses required in 20 (53%)
  - It is “practical and effective” home treatment

J Paed Child Health 2006:42:108-111

Mini-Dose Glucagon at Camp

- Arizona Diabetes Camp 2003
  - Average of 4 episodes/day of severe hypoglycemia for 28 episodes in 1 week
    - ¾ treated with oral glucose
    - 7 children received GCG
      - 2 had seizures and were given 1 mg GCG
      - 5 children were alert and received Mini-Dose GCG
  - BG before GCG 42.3 +/- 9.2 mg/dL
  - BG after GCG 152+/- 18.3 mg/dLby 15 min
  - All returned to normal activity after 30 minutes

Hasan and Kabbani. J Pediatr 2004:144:834

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Prospective Study
- Camp Conrad-Chinnock, San Bernardino Mountains, Southern California
- Summer 2009

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Camp Medical Staff
  - Joan Cervisi PNP, CDE
  - Keirsten Montgomery PNP
  - Francoise Sutton, PNP
  - Debbie Warner RN, CDE
  - Peggy Scoggin, RN, CDE
  - Heather Speer, MPH CCRC
  - Susan Clark, MD

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Study Group
  - Campers ages 13-17
  - Mean age 14.9 years
  - All with DM1
  - 65 of 116 campers participated
    - Males 26
    - Females 39

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Introduction
  - Hypoglycemia is the most frequent acute complication of Type 1 diabetes (DM1) during camp
  - Standard treatment
    - 4-6 oz of juice
    - Snack with carbohydrate and protein
  - Emergency treatment
    - Glucagon 1 mg IM

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Retrospective Study, Summer 2008
  - 149 campers with Type 1 DM age 13-17
  - 75 episodes of hypoglycemia (BG <60) in 43 campers. Repeat episodes occurred in 32.
  - Campers on pumps had significant lower HgbA1c $p<0.01$
    - Using pump: mean 7.78%
    - No pump: mean 10.66%

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Retrospective Study, Summer 2008
  - 20% of hypoglycemic episodes occurred on Day 1 of camp
  - 35% of episodes occurred on Days 4 and 5
  - 68.2% of episodes occurred between 8 PM and Midnight

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Retrospective study, Summer 2008
  - Compared GCG doses (100 mcg to 200 mcg)
    - The lower the BG, the more likely the 200 mcg dose was used $p < .001$
      - 100 mcg: Mean BG 52.5 +/- 9.7 mg/dl (2.9 +/- 0.54)
      - 200 mcg: Mean BG 42.3 +/- 5.5 mg/dl (2.35 +/- 0.30)
    - Post GCG BG was higher with 200 ug dose $p<.05$
      - 100 mcg: Mean BG 108 +/- 27 mg/dl (6 +/- 1.5 mmole/l)
      - 200 mcg: Mean BG 135.8 +/- 47.3 mg/dl (7.5 +/- 2.6)

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Purpose
  - Determine the response to treatment of hypoglycemia requiring immediate treatment but not requiring assistance of another person
- Statistical Analysis
  - Group differences by T-Test
  - Frequencies of hypoglycemia – Percentage %

Low Dose Glucagon for Non-Emergent Hypoglycemia

- During camp there is frequent hypoglycemia both daytime and nighttime
  - BG levels are checked on campers at night between midnight and 2 AM
    - All campers the first night
    - Campers who have BG <100 at bedtime
    - Campers with a history of low BG at night
    - Any camper who wishes to be checked
  - It is standard procedure to lower all camper's basal and bedtime insulin by 10-15%

Low Dose Glucagon for Non-Emergent Hypoglycemia

- Methods
  - Campers with blood glucose (BG) <60 mg/dl were offered
    - SQ dose of Glucagon (100 or 200 mcg) plus 4-6 oz of juice OR
    - Standard treatment with 4-6 oz juice plus a snack
  - BG was checked
    - Before treatment
    - 10-15 minutes after treatment
    - Before the next meal

Low Dose Glucagon for Hypoglycemia - Results

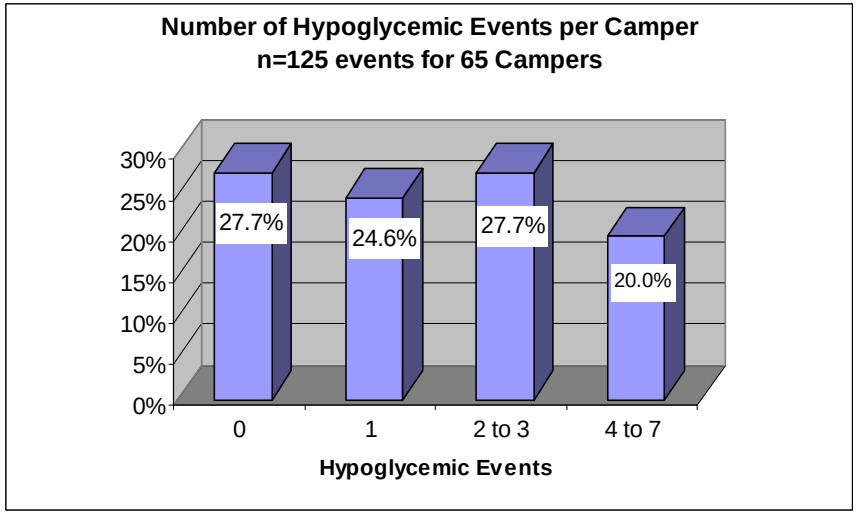
- HgbA1c
  - Mean A1c was 8.2% SD 1.3%
  - Range for A1c 6.4% - 12.4%
  - No difference between males and females
- Campers on pumps – 81.5%
  - On pumps - A1c 7.8% SD 0.8%
  - Injections – A1c 9.7% SD 1.8%
  - Statistically significant p=.004

Low Dose Glucagon for Hypoglycemia - Results

- HgbA1c
  - 83% of campers lowered their basal rates and bedtime insulin at the beginning of camp
    - Lowered insulin – A1c 8% SD 1.2%
    - Did not lower insulin – A1c 9.2% SD 1.6%
  - Statistically significant difference p=.007

Low Dose Glucagon for Hypoglycemia - Results

- Hypoglycemic events
  - No events 18/65
  - With low BG 47/65
- Total hypoglycemic events – 125
  - One episode 16 /47
  - 2-3 episodes 18 /47
  - 4-7 epsidoes 13 /47



Low Dose Glucagon for Hypoglycemia - Results

- Frequency of Hypoglycemic Events
  - Most occurred in the first 4 days of camp
    - Day 2 – 24.8%
    - Day 4 – 29.6%

Episodes by Camp Day		
Day	Frequency	Percent
1	13	10.4%
2	31	24.8
3	26	20.8
4	37	29.6
5	18	14.4
Totals	125 Events	100%

Low Dose Glucagon for Hypoglycemia - Results

- Time of Day of Hypoglycemia
- 38.4% occurred between 2000 and 2400 hours
- 32% occurred between 1400 and 1800 hours
- Activity Times!

TIME OF DAY	FREQUENCY of HYPO EVENTS	PERCENT
0 to 759	11	8.8%
800 to 959	11	8.8
1200 to 1359	10	8.0
1400 to 1759	40	32
1800 to 1959	5	4.0
2000 to 2400	48	38.4
Total	125	100.0%

Low Dose Glucagon for Hypoglycemia - Results

- Hypoglycemic Events – 125 events in 65 campers
- The mean BG was 55.7 mg/dl, SD 9.2 with range of 20-69 mg/dl (3.1 mmole/L, SD 0.51, range 1.1-3.8 mmole/L)
- The mean BG after treatment was 87.9 mg/dl (4.9 mmole/L) SD 27.3 (1.5 mmole/L) ?range

Low Dose Glucagon for Hypoglycemia - Results

- Hypoglycemic events – 125 in 65 campers
  - 47 (37.6%) were treated with Low Dose Glucagon plus juice or glucose tablets
  - 75 (60%) were treated with juice or glucose tablets followed by a snack
  - Time of repeat BG was recorded in 104/125
    - 67% had BG repeated within 10 minutes
    - 82% had BG repeated within 16 minutes

Low Dose Glucagon for Hypoglycemia - Results

- Glucagon versus Oral Treatment (data only on those with follow up BG in 16 minutes)
- 82% of episodes retested in 16 minutes
  - GCG Rx higher BG
  - GCG Rx greater increase in BG

Difference of BG Levels Treated with GCG vs Oral Treatment			
BG levels (mg/dl)	Treatment with GCG	Oral treatment only	p value
BG before Treatment	50.2 SD 8.5	59.1 SD 7.9	<.001
BG after treatment	94.1 SD 28.0	84.0 SD 26.3	.046
BG 16 minutes after RX	96.6 SD 27.1	79.7 SD 23.3	.003
Increase in BG	45.1SD 29.4	21.8 SD 24.0	<.001

Low Dose Glucagon for Hypoglycemia - Results

- Glucagon Treatment versus Oral Treatment
  - The mean BG was lower for the Glucagon treated episodes p=<.001
  - BG after Glucagon treatment was higher than oral treatment p=.046
  - BG 16 minutes after treatment was higher for the Glucagon treated group p=.003
  - Increase in BG was higher following Glucagon p=<.001

Low Dose Glucagon for Hypoglycemia - Summary

- Low Dose Glucagon treatment for non-emergency hypoglycemia is safe and effective
  - There were no significant side effects
  - BG rose more briskly and to a higher level with glucagon treatment

Low Dose Glucagon for Hypoglycemia - Summary

- Hypoglycemia requiring immediate treatment is a common event at diabetes camp
  - The most common time of day was 8 PM to Midnight
  - The second most common time was 2-6 PM
  - Most episodes occurred in the first 4 days of camp

Low Dose Glucagon for Hypoglycemia - Conclusions

- Treatment with Glucagon allowed campers to return to normal activitites more promptly than standard oral treatment
- Low dose Glucagon is a useful and safe treatment for non-emergent hypoglycemia at diabetes camp