Hypoglycaemia

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Content

* What is hypoglycaemia
* Current research
* Hypoglycaemia unawareness
A plasma glucose concentration of less than or equal to 3.9mmol/L

**Classification**
- Severe – requiring assistance
- Documented symptomatic
- Asymptomatic
- Probable symptomatic
- Pseudo-hypoglycaemia

*(Journal of Clinical Endocrinology Metabolism April 2013)*
Common causes of hypoglycaemia

- Too much medication
  - Insulin
  - Sulphonylureas
- Insufficient carbohydrate
  - not enough content
  - delayed
  - vomiting
- Unplanned exercise
- Alcohol
- Marijuana
* **Adrenergic** 3.2 – 3.6 mmol/L  
  * Shakiness & anxiety  
  * Palpitations, tachycardia  
  * Sweating, Pallor, pupil dilation

* **Neuroglycopaenic** < 3.0 mmol/L  
  * Abnormal mental state  
  * Fatigue  
  * Ataxia  
  * Paresthesia, paralysis, headache and amnesia  
  * Seizures

(Textbook of Diabetes, Williams & Pickup 2006)
Mild neuroglycopenia

Cognitive dysfunction

Activation of autonomic symptoms

Severe neuroglycopenia

Sweating, tremor, etc.

Unconscious

Convulsions

Coma/death

Time

Blood glucose (mmol/l)
**Physiology**

**Hypoglycaemia**
- Insulin inhibition
  - Hypothalamus
  - Increased sympathetic nerve activity
- Vasopressin
- ACTH
- Cortisol
- Adrenaline
  - Increased cardiac output
  - Vasodilatation in muscle
  - Vasoconstriction in skin

Blood flow diverted to:
- Brain
- Muscle
- Liver

**Rise in blood glucose**

- Glucagon
- Growth Hormone
- Gluconeogenesis
- Glycogenolysis
- ~3.6mmol/L
- ~5.6mmol/L
International treatment recommendations

* Recommendations for the treatment of hypoglycaemia in Type 1 diabetes universally differs in both quantity and type
* A literature review showed limited ‘evidence based’ methods for current treatments
* 15 gm (Australia, New Zealand & Singapore)
* 10 – 20gm (UK)
* 15 – 20gm (USA)
* 15 – 30 gm (Europe)
* These recommendations are largely ‘based on clinical opinion’

15 grams of study treatment
Consider

- Blood volume is approximately 7% of weight
  (Physics of the Body. 2nd ed. 1999)
Blood volume difference?
I believe people with Type 1 diabetes routinely under treat their hypoglycaemia episodes by following international guidelines based on ‘expert opinion’
Effective treatment of hypoglycaemia in children with type 1 diabetes: A randomised controlled clinical trial

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¹Diabetes and Endocrinology, Capital and Coast District Health Board, Wellington, New Zealand ²Paediatrics, University of Otago Wellington, New Zealand
The treatment of hypoglycaemia in children universally differs in both quantity and type.

Parents often ask about effective alternatives to glucose tablets.

A literature review showed limited ‘evidence based’ methods for current treatments.

ISPAD, APEG, NICE, ADA & CDA recommend 5 - 20g simple CHO followed by 10g of complex CHO.

These recommendations are mainly based on the work of Slama (Arch Intern Med. Vol 150, March. 1990) in adults, extrapolated to children.
In children, treatment with “Mentos dragees” more rapidly resolves hypoglycaemia without rebound hyperglycaemia compared to other commonly used treatment methods such as jelly beans, Just Juice (Orange) and glucose tablets.
43 (8-12 year old) children with type 1 diabetes attending the 2008 National Children’s (5 day) Diabetes Camp
- Parental consent and child assent were obtained
- Height and weight obtained on arrival
- 0.3 g/kg of treatment was calculated for each treatment option (ADA Nutritional Principles Diabetes Care 25:148-198, 2002)
- Recorded on child’s blood glucose chart and supplied to each Camp Leader
- Camp Leaders were research protocol trained
Results

- 191 documented episodes in 39 children
- 1 – 12 episodes per child
- 2 exclusions
- Several pump patients received double treatments according to pump protocol
- 165 single treatments also analysed
  - no significant difference to entire group
Results

Mean blood glucose over time

- Glucose tablets
- Just Juice (Orange)
- Jelly beans
- Mentos dragees

P = 0.099 at 10 mins and p=0.026 at 15 mins between the groups
Results

Mean change in blood glucose over time

P = 0.034 at 10mins and p = 0.005 at 15 mins between the groups
Results

Mean blood glucose over time

$P = 0.099$ at 10 mins and $p = 0.026$ at 15 mins between the groups
Results

Frequency of retreatment

P=0.058 for Jellybean single treatment
Conclusions

* Jellybeans were significantly less effective than the other three treatments used in the study
* Treatments with 0.3 g/kg glucose containing preparations effectively resolves hypoglycaemia in most children by 10 minutes and raises bgl’s by 2 - 2.5mmol/L in 15 minutes
* Symptom relief takes greater than 10 minutes
Effective treatment of hypoglycemia in children with type 1 diabetes: a randomized controlled clinical trial

Can these results translate to adults?
WEIGHT-BASED TREATMENT IS MORE EFFECTIVE FOR RESOLVING HYPOGLYCAEMIA IN ADULTS: A RANDOMISED TRIAL

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\(^1\)Diabetes and Endocrinology, Capital and Coast District Health Board, Wellington, New Zealand
\(^2\)Paediatrics, University of Otago Wellington, New Zealand
A weight-based hypoglycaemia treatment protocol of 0.3 gm/kg is more effective than standard advice in resolving hypoglycaemia and avoiding excessive rebound hyperglycaemia in children with Type 1 diabetes; can this be effectively translated to adults?
Methods

* 30 subjects with Type 1 diabetes
* Consent was obtained on enrolment
* Baseline data collected on arrival
* Treatment quantities were calculated for each protocol - 0.2g/kg, 0.3g/kg and the control of 15 grams in Dextro tablets
* Calculations were recorded in subject’s study file and blood glucose record forms to be mailed back
* All subjects were trained on each protocol
Treatment protocols were randomly assigned by sealed envelope – 5 treatments for each group

Hypoglycaemia was defined as a blood glucose below 4 mmol/L on a Accuchek Nano meter

Blood glucose levels were measured at time 0, & 10 minutes

If hypoglycaemia persisted, treatment was repeated at 10 minute intervals

Advised to have 20g complex CHO after resolution
Results

- 418 documented episodes
- 34 subjects – 21 male & 13 female
- Aged 22 – 71 years
- 1 exclusion for a protocol violation (4 episodes)
- 2 subjects withdrew
- 395 single treatments analysed
- 101 re-treatments
- 18 re-treatments two times
## Results summary

<table>
<thead>
<tr>
<th></th>
<th>0.2g/kg</th>
<th>0.3g/kg</th>
<th>15g (control)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glucose at 10mins (mmol/L)</strong></td>
<td>Mean</td>
<td>4.289</td>
<td>4.667</td>
<td>4.371</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>4.122-4.451</td>
<td>4.459-4.876</td>
<td>4.204-4.539</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.941</td>
<td>1.252</td>
<td>0.986</td>
</tr>
<tr>
<td><strong>Change in glucose (mmol/L)</strong></td>
<td>Mean</td>
<td>1.146</td>
<td>1.483</td>
<td>1.251</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>0.993-1.300</td>
<td>1.285-1.680</td>
<td>1.083-1.419</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.892</td>
<td>1.186</td>
<td>0.990</td>
</tr>
</tbody>
</table>
Results

Mean change in blood glucose over 10 minutes

- 0.2 gm/kg
- 0.3 gm/kg
- control 15gms

P = 0.023 at 10 mins between the groups
Results

Mean rise in blood glucose over 10 minutes

P = 0.641 at T0 and P = 0.009 at 10 mins between the groups
Results

Frequency of re-treatments

- 1 treatment: 127, 139, 129
- 2 treatments: 33, 35, 33
- 3 treatments: 5, 5, 8

Categories:
- 0.2/g/kg
- 0.3g/kg
- 15g (control)
We conclude that a weight based protocol of using 0.3 grams of glucose per kilogram of body weight is the most effective for treating symptomatic hypoglycaemia in adults with type 1 diabetes, and is more effective than the current recommendation of 15 g glucose in all patients.

Blood glucose levels can be expected to raise by 1.5mmol/L in 10 minutes.
Research: Treatment

Weight-based hypoglycaemia treatment protocol for adults with Type 1 diabetes: a randomized crossover clinical trial

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Accepted 9 February 2015
Recent policy changes

Default position is to treat adult hypoglycaemia with 30 grams glucose solution

Treat children with 0.3 grams /kg

We currently have a similar study running in people with Type 2 diabetes

Mean levels of plasma glucose and serum free insulin following experimental intervention before time 0 and ingestion of test foods at time 0.
HypoPak
80ml
15g glucose per pouch

HypoPak
Gluten Free

For treatment of an acute Hypoglycaemia Episode

Gluten and Dairy Free

Note: If hypoglycaemia persists then please seek medical advice

Produced by AJW Enterprises NZ Ltd
The WHiP study

(Weight-based Hypoglycemia treatment in Pumps study)
## Adult

<table>
<thead>
<tr>
<th>Number of first treatments</th>
<th>Episode NOT resolved</th>
<th>Episode resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control N=67</td>
<td>27 (40.3%)</td>
<td>40 (59.7%)</td>
</tr>
<tr>
<td>Weight-based N=77</td>
<td>14 (18.2%)</td>
<td>63 (81.8%)</td>
</tr>
</tbody>
</table>

## Child

<table>
<thead>
<tr>
<th>Number of first treatments</th>
<th>Episode NOT resolved</th>
<th>Episode resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control N=69</td>
<td>26 (37.7%)</td>
<td>43 (62.3%)</td>
</tr>
<tr>
<td>Weight-based N=69</td>
<td>13 (18.8%)</td>
<td>56 (81.2%)</td>
</tr>
</tbody>
</table>
### Response to treatment

Estimates of treatment differences (by linear mixed model)

<table>
<thead>
<tr>
<th></th>
<th>Glucose weight-based minus control Estimate (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adults</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time 10</td>
<td>0.33 (0.005 to 0.66)</td>
<td>0.047*</td>
</tr>
<tr>
<td>Time 20</td>
<td>0.78 (-0.02 to 1.57)</td>
<td>0.055</td>
</tr>
<tr>
<td>Time 30</td>
<td>1.28 (0.57 to 1.99)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td><strong>Children</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time 10</td>
<td>0.45 (0.18 to 0.72)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Time 20</td>
<td>0.15 (-0.62 to 0.91)</td>
<td>0.7</td>
</tr>
<tr>
<td>Time 30</td>
<td>0.44 (-0.47 to 1.35)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

* A significant difference between the groups
Hypoglycaemia unawareness
Hypoglycaemia unawareness

- In the absence of symptoms
- In those trying for normoglycaemia
- HBA1c < 40 mmol/mol
- Frequent hypoglycaemia
- Is extremely dangerous
Contributing factors

- Especially seen in Type 1 of long duration
- Autonomic neuropathy
- Glucose receptors in hypothalamus
- Masking medicines
Treatment

* Aim for higher blood glucose targets
* More accurate CHO counting
* Avoid over correcting (or stacking)
* Test more frequently (and react)
* Adjust insulin doses
* Test before driving
* Consider CGMS to look at 24 hour patterns
Any questions?