Hypoglycaemia:
Will a bit of sugar will sort it?
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Disclosures

Honoraria and expenses received from:

○ Astra Zeneca
○ Sanofi
○ Novo Nordisk
○ Boehringer Ingelheim
○ Lilly

○ Napp
○ Janssen
○ MSD
○ Mylan
○ Pfizer
Learning Objectives

By the end of this session you will:

○ Know the definition of a hypo
○ Understand the strategies to prevent hypoglycaemia
○ Outline the medical and non-medical treatment of hypos
○ Discuss the new treatments available
What IS Hypoglycaemia?

What exactly am I looking at?
Signs and symptoms

- Feeling tearful
- Headache
- Lack of concentration
- Lips feeling tingly
- Palpitations and a fast pulse
- Trembling and shaky

- Anxious or irritable
- Blurred sight
- Sweating
- Hunger
- Going pale
- Tiredness

Source: Diabetes UK
Why do hypos happen?

- Missing or delaying a meal or snack
- Not having enough carbohydrate at your last meal
- Exercise without extra carbohydrate or reducing insulin dose
- More insulin / medication than needed
- Drinking alcohol

Best non-medication treatment is taking steps to prevent hypos

Source: Diabetes UK
Practice vs trials

○ NICE and DVLA: <4 mmol/L
○ ADA/EASD: <3.9 mmol/L
○ In trials: no defined definition. Usually:
  ○ blood glucose 3.1-3.9 mmol/L (mild)
  ○ blood glucose <3.1 mmol/L (severe)
  ○ BUT what about assistance?
○ Severe heterogeneity

○ Can lead to difficulty in predicting frequency associated with medications and improvement associated with treatment

Hypoglycaemia in the UK

- Rate of any hypoglycaemic event
  - **73.3** events per patient-year for type 1 diabetes (T1DM)
  - **19.3** events per patient-year for type 2 diabetes (T2DM) treated with insulin

- Estimated cost range:
  - Up to £2,152 for severe episodes (admission to hospital)
  - As low as £1.67 for non-severe episodes

- Total estimated NHS cost of managing insulin-related hypoglycaemia is £468.0m per year

Source: Khunti, 2016, Parekh, 2015
Treatment

As simple as giving glucose?
Non-medication treatment

- Blood sugar is < 4mmol/L or hypo symptoms:
  - Sugary drink or snack
    - small glass of non-diet fizzy drink or fruit juice
    - a small handful of sweets (jelly babies)
    - 4 or 5 dextrose tablets.
  - Test blood sugar after 10 to 15 minutes
    - >4mmol, have a carbohydrate snack
    - <4mmol, treat again then test in 10 to 15 minutes
  - Carbohydrate-containing snack or meal e.g. a slice of toast, biscuits, glass of milk

15:15 rule
15g then 15 mins
Costs to Patient

- Jelly babies
  - £1.48 / bag
  - 87 Kcal / 4 sweets

- Lift
  - £1.30 / 60mL shot
  - 57 Kcal / shot

- Dextrose tabs
  - £0.89 / 10 tabs
  - 64 Kcal / 4 tablets

- Can of Coke
  - £0.99 / can
  - 150 Kcal / can

- Fear and anxiety
- Embarrassment
- Loss of productivity
- Weight gain
- Uncontrolled glucose (rebound hyperglycaemia)
Medication

- Reserved for severe hypoglycaemia (unconscious or unable to eat/drink)
- SC or IM Glucagon 1mg

- Follow with sugary drink or snack, followed by a carbohydrate-containing snack

*Or if no response in 10 minutes*

- IV dextrose infusion

Source: Diabetes UK
Glucagon

○ Reliant on glycogen stores
○ Avoid use in:
  ○ prolonged fasting
  ○ adrenal insufficiency
  ○ phaeochromocytoma
  ○ chronic hypoglycaemia
  ○ alcohol induced hypoglycaemia
○ Can be repeated once

Pic source: Wikimedia Commons. Author: C. Muessig
Glucagon administration

- Remove seal
- Inject contents into vial
- Swirl vial until contents is clear
- Use same syringe to withdraw all liquid
- Give fast acting sugar and then a CHO snack
- Remove the needle cover and push into vial
- Inject into arm, buttock or thigh

Source: [http://www.lillyglucagon.com/how-to-use](http://www.lillyglucagon.com/how-to-use)
The Future

As simple as giving glucagon?
Gvoke PFS / Hypopen

- First ready-to-use liquid formulation available
- Approved by FDA in September 2019
- Currently a pre-filled syringe. Auto-injector available in 2020
- Positive results from Phase 3 clinical trials in severe hypoglycaemia in both children (n=30) and adults (n=154).
  - There was a 100% treatment success rate in children, and a 99% success rate in adults.

Source: [https://www.gvokeglucagon.com/hcp](https://www.gvokeglucagon.com/hcp)
Another way?

- Baqsimi®
- Insert tip into one nostril and press the device plunger all the way in until the green line is no longer showing
- The dose does not need to be inhaled

- U.S. list price for nasal glucagon is $280.80 for one-pack. Injections start at $145
- UK glucagon injection is £11.52
- EMA approval Oct 2019
Clinical Evidence

- Non-inferiority to glucagon injection in treating insulin-induced hypoglycemia in adults
  - Two randomised, multicenter, open-label, 2-period crossover trials: 3 mg nasal dose vs 1 mg IM dose.
  - Study 1: 70 adult patients with T1DM
  - Study 2: 83 adult patients with T1DM or T2DM

Source: [https://www.baqsimi.com/hcp/adult/clinical-trials](https://www.baqsimi.com/hcp/adult/clinical-trials)
Clinical Evidence Cont.

- Mean plasma glucose concentrations over time with nasal or IM glucagon
  - 66 patients with T1DM
  - Proportion achieving increase in plasma glucose to ≥70 mg/dL or increase of ≥20 mg/dL from glucose nadir within 30 minutes

Source: https://www.baqsimi.com/hcp/adult/clinical-trials
Delay in response?

- Slight delay in glycaemic response (5 mins)
- Clinically inconsequential
- Offset by the time required, errors, and failures to deliver among nonmedical caregivers
- Recent study showed nasal delivery of glucagon is much faster with a higher success rate
  - trained caregivers (16s vs. 1.9 min for time to administer, 94% vs. 50% for delivery)
  - untrained acquaintances (26s vs. 2.4 min, 93% vs. 20% for delivery)

Source: Yale et al. EASD Poster, 2015
Summary

- There is no consistent definition of hypoglycaemia in trials which can make frequency difficult to interpret.
- There is considerable cost to the NHS and patients, although these are often measured differently.
- Non-medical treatment can be inconsistent and not always appropriate.
- Current medical treatment is underused and can be difficult for carers to administer.
- New formulations offer opportunity for improved treatment of severe hypoglycaemia.
- Clinical evidence demonstrates no discernible difference between IM and nasal administration.
“Prevention is better than cure”

- Erasmus
Thanks!

Any questions?
References

- Presentation template by SlidesCarnival

- [https://www.nhs.uk/conditions/low-blood-sugar-hypoglycaemia/](https://www.nhs.uk/conditions/low-blood-sugar-hypoglycaemia/)


