Hypoglycaemia:

Will a bit of sugar will sort it?

Vicky Ruszala

Specialist pharmacist in Diabetes and Endocrinology at North Bristol NHS Trust

You can find me at:

@VixRz

Disclosures

Honoraria and expenses received from:

- *Astra Zeneca*
- *Sanofi*
- *Novo Nordisk*
- *Boehringher Ingelheim*
- *Lilly*
- *Napp*
- *Janssen*
- *MSD*
- *Mylan*
- *Pfizer*

Learning Objectives

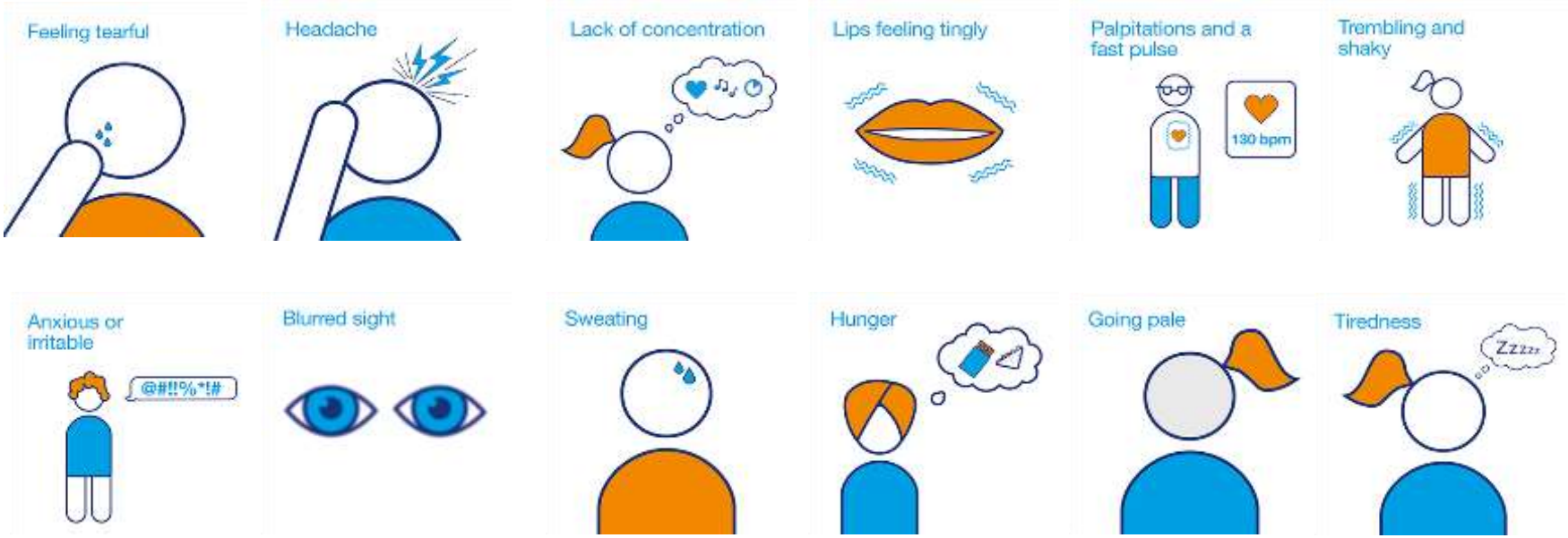
By the end of this session you will:

- *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



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

Source: Balijepalli C, et al. Clin Epidemiol 2017

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

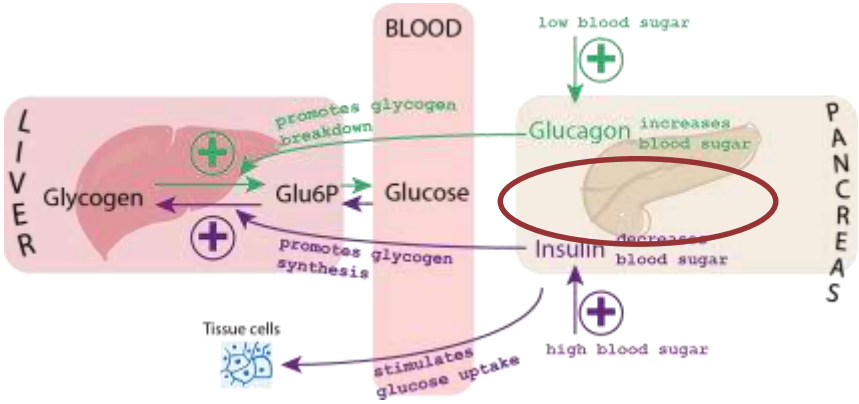
Or if no response in 10 minutes

- 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

Remove the needle cover and push into vial

Inject contents into vial

Swirl vial until contents is clear

Use same syringe to withdraw all liquid

Inject into arm, buttock or thigh

Give fast acting sugar and then a CHO snack

Source: 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

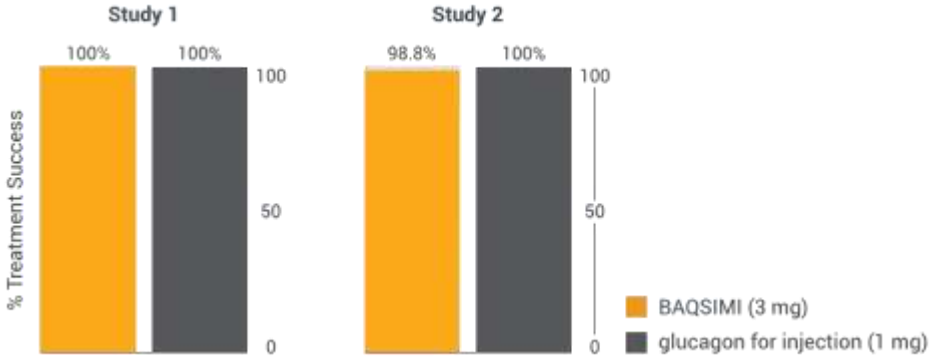
Another way?

- 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

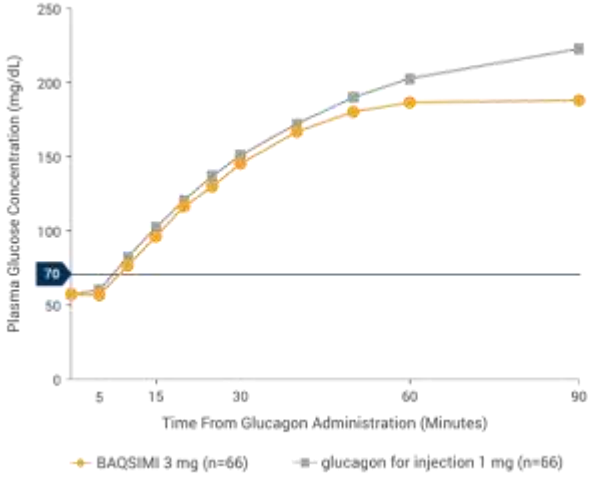
- Non-inferiority to glucagon injection in treating insulin-induced hypoglycemia in adults
  - Two randomised, multicenter, open-label, 2-period crossover trials: 3 mg nasal dose vs1 mg IM dose.
  - *Study 1*: 70 adult patients with T1DM
  - *Study 2*: 83 adult patients with T1DM or T2DM



Source: https://www.baqsimi.com/hcp/adult/clinical-trials

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/
- Balijepalli C, Druyts E, Siliman G, et al. *Hypoglycemia: a review of definitions used in clinical trials evaluating antihyperglycemic drugs for diabetes.* Clin Epidemiol 2017. 23;9:291-296. eCollection 2017.
- Khunti K, Alsifri S, Aronson R , et al*. Rates and predictors of hypoglycaemia in 27 585 people from 24 countries with insulin-treated type 1 and type 2 diabetes: the global HAT study. Diabetes Obes Metab 2016;18:907–15.doi:10.1111/dom.12689*
- Parekh WA, Ashley D, Chubb B , et al*. Approach to assessing the economic impact of insulin-related hypoglycaemia using the novel local impact of hypoglycaemia tool. Diabet Med 2015;32:1156–66.doi:10.1111/dme.12771*
- Rickels MR, Ruedy KJ, Foster NC, Piché CA, Dulude H, Sherr JL, Tamborlane WV, Bethin KE, DiMeglio LA, Wadwa RP, Ahmann AJ, Haller MJ, Nathan BM, Marcovina SM, Rampakakis E, Meng L, Beck RW; T1D Exchange Intranasal Glucagon Investigators. *Intranasal Glucagon for Treatment of Insulin-Induced Hypoglycemia in Adults With Type 1 Diabetes: A Randomized Crossover Noninferiority Study*. Diabetes Care. 2016 Feb;39(2):264-70. doi: 10.2337/dc15-1498. Epub 2015 Dec 17.
- Yale JF, Piche C, Lafontaine M, et al. *Needlefree nasal delivery of glucagon is superior to injectable delivery in simulated hypoglycaemia rescue.* Poster presented at European Association for the Study of Diabetes (Abstract). Stockholm, Sweden, September 2015. Available from http://www.easdvirtualmeeting.org/resources/needle-free-nasal-delivery-of-glucagon-is-superior-to-injectable-delivery-in-simulated-hypoglycaemia-rescue--3. Accessed 3 December 2015
- Gvoke. https://www.gvokeglucagon.com/hcp Accessesd 25/10/19
- Baqsimi. https://www.baqsimi.com/hcp/adult/clinical-trials Accessed 25/10/19