# Toxicology case 2

Dr Sammi Pe

QMH

Nov 2011

# Hx

- 03:38am
- 35/M
- Good PH
- Poly-substance abuser of cannabis, Methamphetamine and cough mixture
- c/o insomnia x 2/12
- Suicidal ideation x 1/12
- Noticed by aunt that pt had DO after gave her “ a photo to use after his death”

# Hx

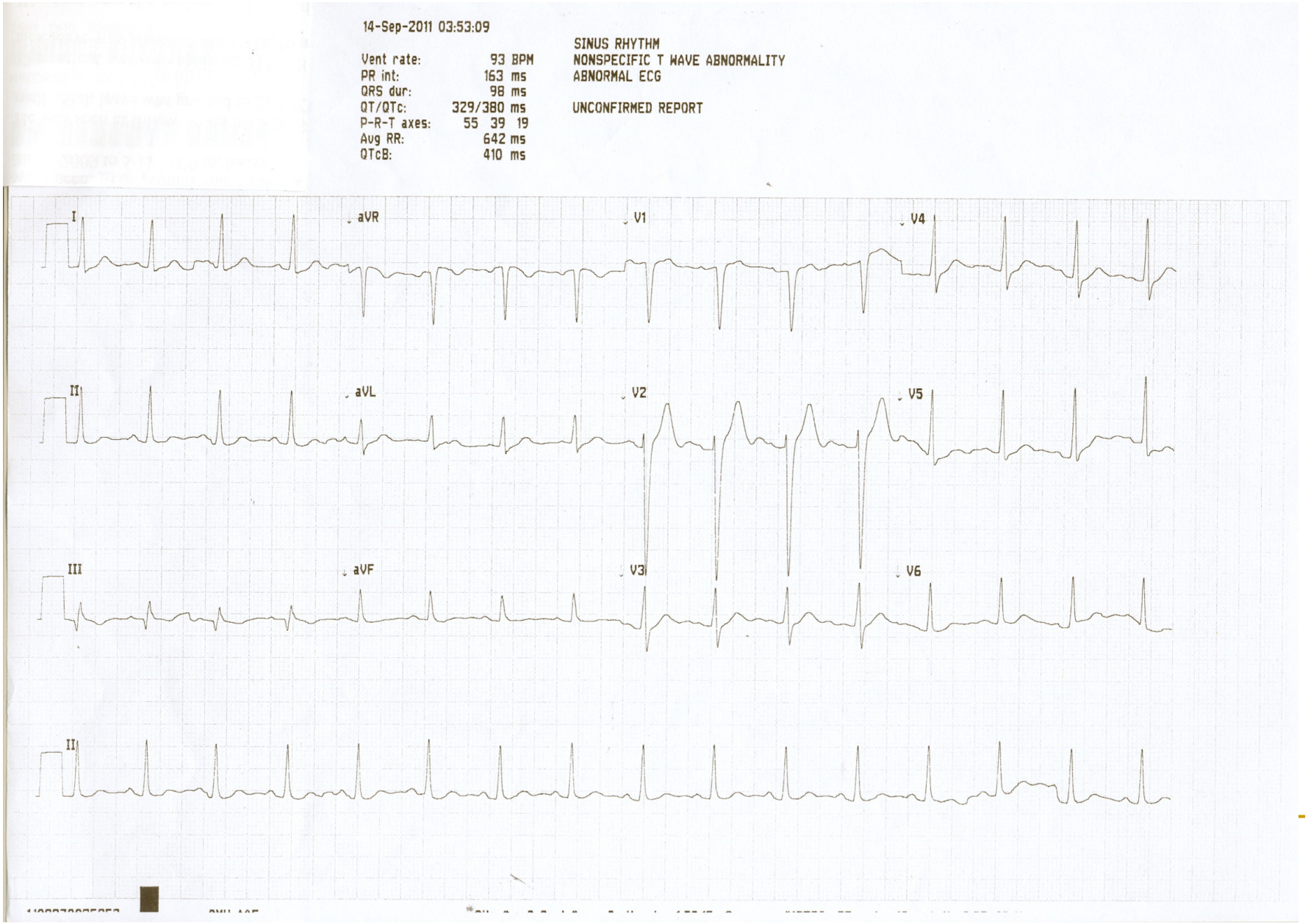
- Claimed taken 120 tabs of Diamicron at 2am
- Aunt also found 12 packs of Diamicron emptied ( 10 tabs /pack, 80mg /tabs)
- Deny alcohol intake
- No vomiting
- Also cut wrist 2/7 ago

# P/E

- GCS 15/15  pupil 3+/3+
- BP 136/82  P 96
- Temp 36.4 ˚C, normal Skin
- H stix 4.3

- Chest Clear
- Abd soft, no bladder, normal bowel sound
- CVS: HS dual , no murmur

# ECG


14-Sep-2011 03:53:09
Vent rate: 93 BPM
PR int: 163 ms
QRS dur: 98 ms
QT/QTc: 329/380 ms
P-R-T axes: 55 39 19
Avg RR: 642 ms
QTcB: 410 ms
SINUS RHYTHM
NONSPECIFIC T WAVE ABNORMALITY
ABNORMAL ECG
UNCONFIRMED REPORT
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

# Condition

- Invariably fatal?
- Potentially fatal?
- Definitely toxic?
- Potentially toxic?
- Non-toxic ingestion?
- Possible exposure?

# What will you do next?

- Basic life support
- Gastric lavage ?
- Activated charcoal ?
- Whole bowel irrigation ?
- Observation only?

# Progress

- GL with 9L NS at ~2hr post-ingestion
  - Ingestion - door time: 1 hr 38 mins
  - Door - GL time : 32 mins
- Food debris + white tablets ruminant found
- Given AC

- Blood x CBC, L/RFT, RG,
- Blood / urine/ GL x toxicology screen

# Progress

- No hypoglycaemic S/S observe during initial management

Admitted EMW x close observation of hypoglycaemia

Initial EM Mx: IDIS Q6H

H stix Q30 mins x4  then Q1H

D50 20ml IV if H stix <4

# Blood test

- i stat: pH 7.37 BE 2 HCO3 27.5
- Na 139 K 3.2 Ur/Cr 9.8/91
- LFT Normal
- WCC 12.8  Hb14
- Blood  screen x panadol / Salicylate / ethanol : Not detectable

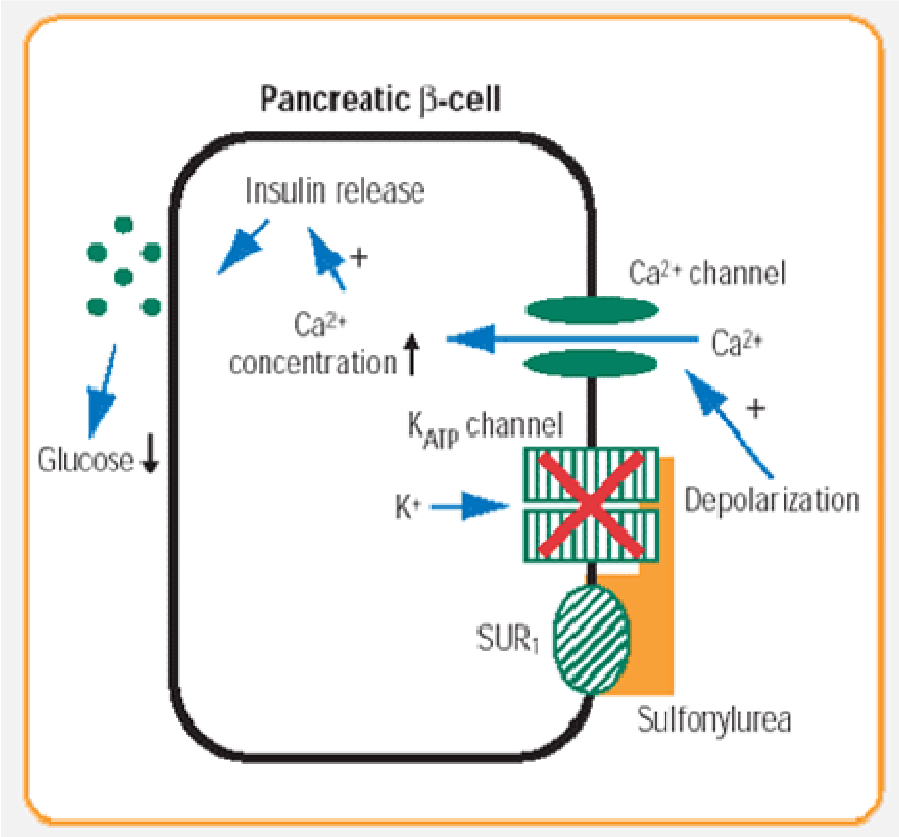
# Overnight Progress

- Repeated Hypoglycaemic attack & require blous D50
- Encourage freq intake ( bedside biscuits as snack given)
- IVF : D10 Q6H

# Sulfonylurea SU

- Oral hypoglycemic agent used to treat DM
- Mechanism: to stimulate the endogenous insulin release from pancreatic $\beta$ cell

| SU | Trade names | Time to peak (hr) | T ½ (hr) | Active metabolite | Duration of action (hr) |
|---|---|---|---|---|---|
| 1st Generation | | | | | |
| Tolbutamide | Diatol, Rastinon | 3-4 | 3-28 | N | 6-12 |
| Chlorproamide | Diabinese | 2-7 | 36 | Y | 60 |
| 2nd Generation | | | | | |
| Glibenclamide Glyburide | Daonil | 2-6 | 10 | N | 12-24 |
| Glipizide | Minidiab, Glucotrol XL | 1-3 | 7 | N | 12-24 |
| Gliclazide | Diamicron | 2-4 | 8-12 | N | 24 |
| Glimepiride | Amaryl, Zoryl | 2-3 | 5-9 | Y | 16-24 |


Pancreatic β-cell
Insulin release
+
Ca2+ channel
Ca2+
concentration
Ca2+
KATP channel
+
Glucose
K+
Depolarization
SUR1
Sulfonylurea

# Clinical Features

- Hypoglycaemia – major concern of its toxicity
- Only 1 tab can result in hypoglycaemia *( esp in Kids & Non-DM patient)*
- Onset of hypoglycaemic S/S can be delayed up to >= 24 hrs
- S/S of Hypoglycaemia
  - CNS: drowsiness, weakness, confusion, coma, seizure, cerebral edema
  - Sympathomimetic: sweating, tachycardia, hypertension

# Investigation

For Suspected drug induced hypoglycaemia

- Serum Glucose
- Serum insulin
- C-peptide
  - ↑ insulin + ↓ C-peptide ➔ exogenous insulin administration
  - ↑ insulin + ↑/N C-peptide ➔ endogenous insulin e.g. insulinoma, SUs, Non-SU secretagogues overdose
- Serum and urine toxicology
- Drugs sample chemical analysis

# Management

- Consider GI decontamination ( GL / AC) in selected case
- Monitoring for hypoglycaemia
- Observation for at least 24 hrs
- Treat with dextrose +/- thiamine and food
- Glucagon ( if failed IV access)
  - stimulate glycogenolysis in liver
  - Inhibit glycogenesis in liver
  - Stimulate glyconeogenesis , ↓ glycolysis
- Octreotide -- if refractory hypoglycaemia
  - Adults 50 µg sc Q6H

# How much dextrose need ?

- Dextrose dosage initially 0.5-1g/kg bolus
  - 40ml D50 = 20g glucose
  - D10 Q6H = 50g/6H = 8.3g /hr
- It is not enough to maintain serum glucose level by give only Dextrose infusion ➔
- **Food** is more important in provide calories
- What to prescribe
  - ? DAT
  - ? High calories intake

# Opinion from Dietitian

- Complex carbohydrate diet Q3H ( day time)
  - e.g. Biscuits, bread, milk

+

- Corn carbohydrate diet before bed
  - e.g. Cereal + milk
  - Keep over-night glucose level more stable

# Octreotide (Sandostatin)


HA 0.05mg/ml $88.57

- An octapeptide analogue of somatostatin
- Potent inhibitor of insulin release via a G protein in the beta islet cell
- Indication
  - Requiring multiple rescue dextrose bolus
  - Refractory hypoglycaemia
- Need to treat with dextrose and food
- Dosing
  - Adult 0.05mg sc Q6H  2-4 days
  - Children 1-1.5 $\mu$g/kg sc Q6H 2-4 days
- Monitor glucose closely for 24 hrs after stopping the octreotide before discharge
- Well tolerate in general
  - Local stinging at site (7%), transient nausea  and later diarrhea ( in doses> 100 µg)

# Should Octreotide be use early ?

TOXICOLOGY/ORIGINAL RESEARCH

## Comparison of Octreotide and Standard Therapy Versus Standard Therapy Alone for the Treatment of Sulfonylurea-Induced Hypoglycemia

**Charles J. Fasano, DO**
**Gerald O'Malley, DO**
**Paul Dominici, MD**
**Elizabeth Aguilera, MD**
**Daniel R. Latta, BS**

From the Department of Emergency Medicine, Albert Einstein Medical Center, Philadelphia, PA.

# Study objective

- Test whether *Octreotide + standard tx* can have better serum glucose level at serial interval in SU–induced hypoglycaemic patients compare with *standard tx* alone

# Method

- Prospective, double-blind, placebo-controlled trial
- All adult pt present to ED with hypoglycaemia (serum glucose <60mg/dL) + taken SU +/- insulin  were screened
- Randomized to
  - Standard + placebo  Vs  Standard + sc octreotide
    - Standard ( 50ml D50 + oral carbohydrate )
    - Placebo (1ml 0.9 % NS)
    - Octreotid (75µg sc)

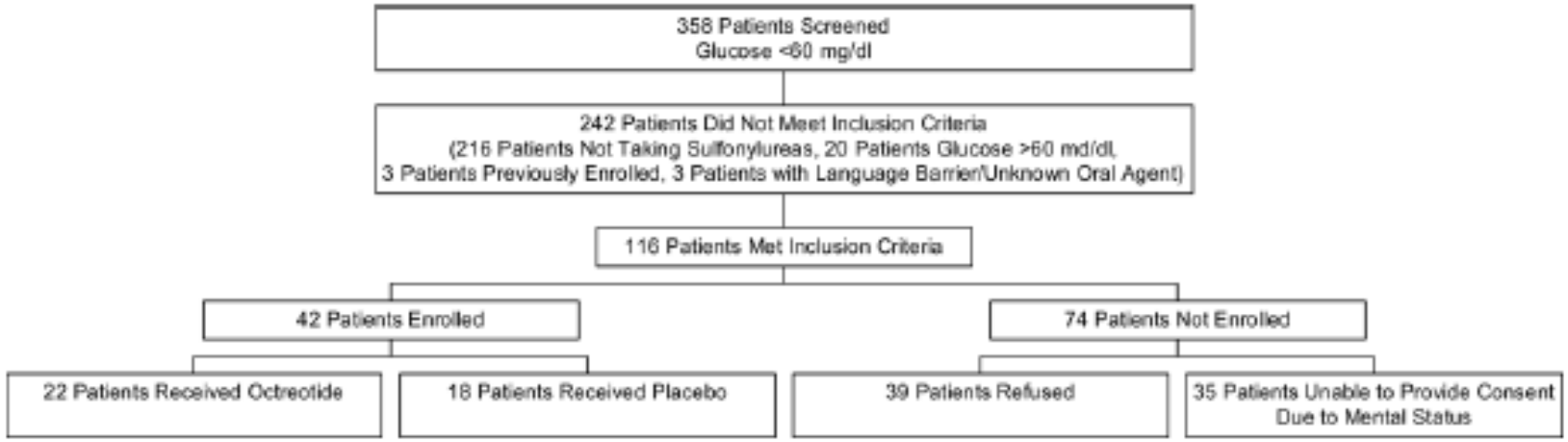



**Figure 1.** Disposition of patients screened for hypoglycemia.

# Result

Total 40 pts

**18 placebo Vs 22 octreotide**

mean Glucose level

At 0hr:

- 35mg/dL ( P Gp)
- 39mg/dL (O Gp)

At 1-8 hrs

- Higher in O gp

subsequent hrs

- no sig difference

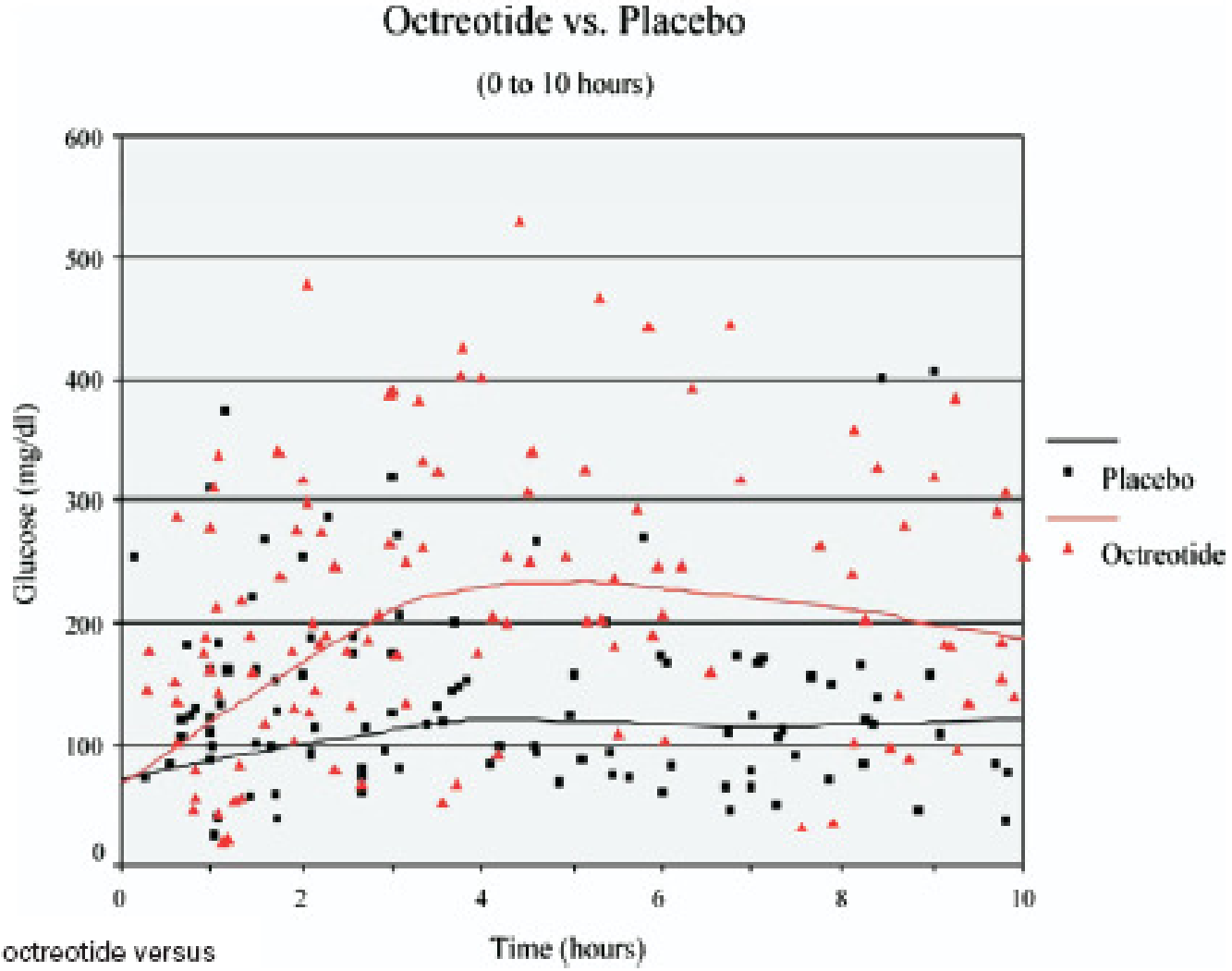



**Figure 2.** Serum glucose octreotide versus placebo.

**Table 2.** Mean difference in serum glucose, octreotide versus placebo.

| Time After Medication Administration, h | Mean Glucose Difference, Octreotide Versus Placebo, mg/dL | 95% CI | *P* Value |
|---|---|---|---|
| 0 | 1 | 59 to 60 | 1.0 |
| 1–3 | 56 | −3 to 115 | .08 |
| 4–8 | 127 | 68 to 187 | <.001 |
| 9–12 | 16 | 43 to 47 | .99 |
| 13–16 | −2 | 61 to 52 | 1.0 |

# Conclusion

- The addition of octreotide to std therapy in SU-induced hypoglycaemia do increase serum glucose level in first 8 hrs
- Recurrent hypoglycaemic episodes occurred less freq in Octreotide Group.

# Use of octreotide acetate to prevent rebound hypoglycaemia in sulfonylurea overdose

Report by Ziauddin Hassan, *Registrar in Emergency Medicine*
Checked by John Wright, *Consultant in Emergency Medicine*
Newcastle General Hospital, Newcastle, UK
doi: 10.1136/emj.2007.051326

Table 2

| Author, country, date | Patient group | Study type | Outcomes | Key results | Study weaknesses |
|---|---|---|---|---|---|
| Boyle *et al*, 1993, USA | 8 healthy volunteers, age range 18–50 years given 1.45 mg/kg glipizide. When glucose had dropped to 50 mg/dl then 50 ml 50% glucose was given followed by either variable dextrose infusion or octreotide. At 5 h a second 50% glucose bolus was administered and the time to return to target glucose value was measured | Experimental study on healthy volunteers | Time to return to target glucose value of 85 mg/dl after second 50% glucose bolus | 3 h vs 6.5 h ($p=0.001$) | Small number, experimental study. Not blinded, subject to bias |
| Mdaughlin *et al*, 1999, USA | 9 patients of whom 6 had taken glyburide OD and 3 glipizide OD. Age range 20–65 years | Observational | Mean number of episodes of hypoglycaemia before and after treatment with octreotide | 3.2 vs 0.2 ($p=0.008$) | Retrospective chart review design. Sample size small |
| | | | Mean number of ampoules of 50% dextrose before and after treatment with octreotide | 2.9 vs 0.2 ($p=0.004$) | |

OD, once daily.

# Our case – in EMW

Noted recurrent hypoglycemic attack while on D10 drip and food

Required episodes of D50 rescue bolus during EMW stay

Consulted ICU for close monitoring

All along conscious

# In ICU

- D50 infusion was given to maintain plasma glucose
- Wean off dextrose infusion gradually on D2
- Transfer back to EMW for further management

- No more hypoglycaemic attack afterward with freq snack and food
- Consulted Psy
- Dx: adjustment disorder , substance abuse
- F123 to PYNEH

# Lesson to learn

- Better diet replacement in EMW
- Early octreotide may reduced the recurrent hypoglycaemic attack → prevent the ICU admission

# Thank you

Special Thx to Dr SH Tsui