The use of Verapamil and Diazoxide in the management of insulinoma

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Objective

To report the successful treatment of a benign insulinoma using diazoxide, verapamil and surgery.

Background

Insulinomas comprise of insulin secreting Islet cell tumours found in the pancreas causing insulin to be continuously released despite low blood glucose levels (BGL). Symptoms include frequent episodes of hypoglycaemia and abdomen pain.

Insulinomas occur in 1-3people in every million each year with 90% being benign (non-cancerous).

Surgical resections including enucleation or partial pancrearectomy have 90% cure rates thus are first line treatments for insulinoma.

Pre-operative management includes giving diazoxide and verapamil to reduce the risk of hypoglycaemia and reduce the need for glucose supplements. There are numerous case studies that demonstrate the effective use of diazoxide and verapamil for management of insulinoma tumours that are non-localised or have failed previous surgery[1,2].

Verapamil

Verapamil is a non-dihydropyridine calcium channel blocker used to prevent calcium influx into hepatic beta cells required for insulin secretion. Verapamil is used to manage low blood sugar levels[3].

Diazoxide

Diazoxide is a non-diuretic benzothiadiazine derivative and works by opening potassium channels causing a hyperpolarisation at the hepatic beta cell membrane. This prevents calcium channels opening hence halting insulin release causing a potent hyperglycaemic effect[4].

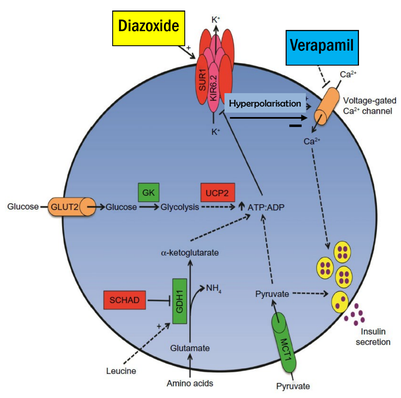

Figure 1: Mechanism pathway of Diazoxide and Verapamil in hyperinsulinism[5]

Case Progression and Interventions

Day 1 Commenced 72-hour monitored fast.

Blood glucose levels of 2.1-3.3mmol/L

Day 4 Calcium stimulation test completed to locate the Insulinoma.

Verapamil 40mg twice a day commenced, then increased to 80mg twice a day for low BGL.

Blood glucose levels subsequently between ~6-7.7mmol/L

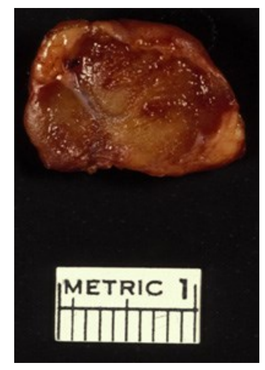

Figure 2: Resected insulinoma[6]

Day 9 Diazoxide 25mg twice a day commenced.

Day 10 Laparoscopic partial pancreatectomy with splenectomy.

Blood glucose levels averaged 10-12mmol/L.

Insulin glargine 14 units daily commenced.

Diazoxide and verapamil were ceased.

6 months Blood glucose levels normalised.

Post-Op Insulin glargine was ceased.

Full recovery with no symptomatic hypo or hyperglycaemic events.

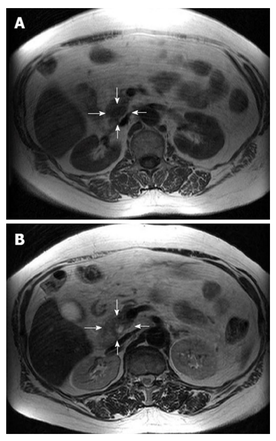

Figure 3: CT scan showing typical location of insulinoma[7]

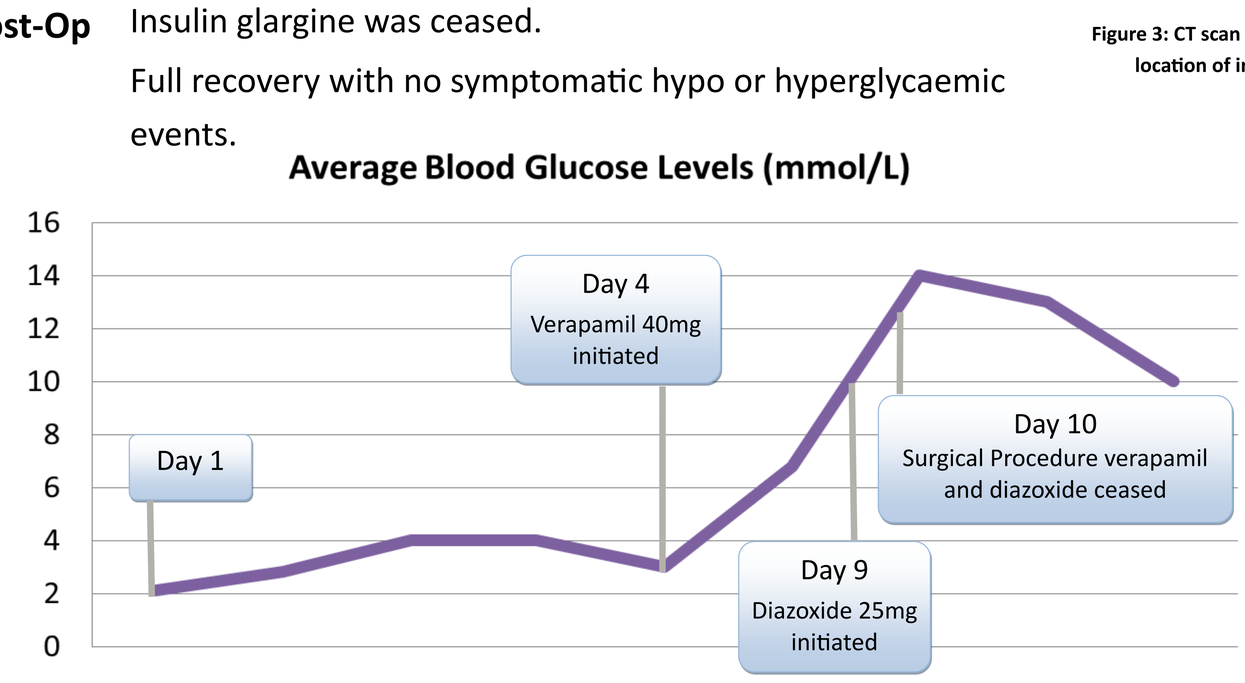

Figure 4: Average Blood Glucose levels of the patient during admission

Clinical Features and Progress

A 38 year old caucasian male, with no known diabetic history, presented to hospital via ambulance with symptoms of hypoglycaemia including confusion, diaphoresis, and finger and toe cramping after going for a run.

BGL on admission was 2.4mmol/L.

His symptoms improved slightly after eating.

He had a past medical history of asthma, hypertension with a family history of prostate cancer and he has experienced unexplained weight loss of 10kg in the previous 3-6 months.

He was not on any regular medications or treatments.

Upon admission our patient underwent investigations with a 72 hour monitored fast. The results of the fast revealed increased levels of insulin, C peptide and proinsulin whilst a CT scan revealed a 19mm pancreatic neuroendocrine tumour, with no evidence of metastatic disease.

A calcium stimulation test was completed to locate the tumour, which was found in the pancreas pressing against his spleen.

Surgical intervention was the preferred course of treatment.

Outcome

Post surgery the patient's BGLs were high. Insulin glargine was commenced to stabilise BGL's. Insulin glargine was gradually weaned over six months under specialist supervision. At six month post the operation he does not require any medications for BGL management, with normal BGLs.

The patient is expected to live a fully functional life with no affect on his longevity.

Conclusion

This case demonstrates that diazoxide and verapamil allowed for control of BGLs until surgical cure in a benign insulinoma.

Our case reinforces that although surgical management remains the first line treatment, medical treatment with diazoxide and verapamil can play a crucial role in the management of unresectable or metastatic insulinoma.

The use of diazoxide and verapamil successfully controlled and prevented insulinoma induced hypoglycaemia allowing the patient to be managed surgically ultimately making a full recovery.

References and Contact

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