Control of plasma glucose with somatostatin analogue (SMS 201-995) during surgical removal of insulinomas

C. Utas, F. Kelestimur, A. Boyaci¹ and A. Saglam²

Departments of Internal Medicine, ¹Anesthesia and ²General Surgery, Erciyes University Medical Faculty, Kayseri, Turkey

Summary: Prevention of hypoglycaemia may sometimes be difficult in the operative period of insulinoma when parenteral volume overload is contraindicated due to severe cardiac failure. We investigated the effects of octreotide on hypoglycaemia during operations in two patients with insulinoma, one of whom had severe congestive heart failure. We found no hypoglycaemic values by using octreotide 100 µg administered subcutaneously one hour before surgery. Octreotide therapy can safely be used before surgery to prevent hypoglycaemia in patients with insulinoma.

Introduction

The primary treatment of insulinoma is surgery. It is well known that hypoglycaemia should be avoided during operation, since it can lead to undesirable effects. The maximum risk of hypoglycaemia is thought to occur following manipulation of the insulin-secreting tumour.¹ In order to prevent this complication, large volumes of glucose-containing solutions are often administered during operation. However, prevention of hypoglycaemia may be difficult when parenteral volume overload is contraindicated due to severe cardiac failure. A new long-acting octapeptide analogue of somatostatin (SMS 201-995, octreotide) which works in insulinoma by inhibiting insulin secretion, has been successfully used in medical treatment of patients with insulinoma.^{2–5}

The purpose of this study was to investigate the effects of octreotide on hypoglycaemia during operation. We have administered octreotide before surgery in two patients with insulinoma, one of whom had severe congestive heart failure.

Patients and methods

Case 1

A 48 year old woman was admitted to the hospital because of convulsions. She was well until 6 months earlier, when hypoglycaemic episodes, some of

which were characterized with convulsions, started. Immunoreactive insulin levels measured at the same time when blood glucose levels were 1.38, 1.65 and 1.21 (mmol/l), were 17.75, 36.50 and 52.19 (N:0–30 µU/ml), respectively. Evidence of insulin mediated hypoglycaemia is shown by plasma insulin levels ≥ 6 µU/ml during hypoglycaemia, while normal persons have lower concentrations.⁶ A computed tomographic (CT) scan of the abdomen showed a suspected small rounded mass on the corpus of the pancreas. The tumour was enucleated totally at operation and histopathological examination confirmed benign insulinoma.

Case 2

A 62 year old woman presented with a 6-year history of episodes of mental confusion, sometimes with seizures associated with hunger and sweating, improving after meals. On hospitalization these symptoms were shown to be associated with hypoglycaemia. The insulin levels were 54.43, 22.57 and 22.75 µU/ml when blood glucose levels were 0.38, 2.31 and 0.44 mmol/l, respectively. The mass seen on CT was removed at operation and histopathological examination revealed benign insulinoma. The patient also had chronic obstructive pulmonary disease and severe congestive cardiac failure characterized by hepatomegaly, pretibial oedema and ascites which were refractory to therapy.

After the diagnosis, octreotide was used in both patients and no hypoglycaemic episode was seen. Octreotide successfully controlled hypoglycaemic episodes on the days before surgery. In other words

Correspondence: Cengiz Utas, M.D., Erciyes University, Medical Faculty, Internal Medicine Department, 38039 Kayseri, Turkey.

Accepted: 27 July 1993

the tumours appeared responsive to octreotide therapy.

A single dose of octreotide 100 µg (Sandostatín, Sandoz) was given subcutaneously one hour before surgery to both of the patients, and glucose profiles were obtained every 15 minutes during surgery. None of the patients required intravenous glucose infusion during surgery.

Plasma glucose levels were measured by glucometer (Ames) using dextrosticks. The simultaneous blood samples were taken and glucose levels were confirmed by AutoAnalyser using the glucose oxidase method. Insulin levels were measured by radioimmunoassay using commercial kits (Diagnostic Production Co., California, USA).

Results

We found no hypoglycaemic values during the operation and postoperative period in both patients. The glucose levels checked after a single dose of octreotide are shown in Table I.

Discussion

Islet cell tumours secreting insulin may be benign or malignant. The elective treatment of benign insulinoma is surgical enucleation of adenoma, or subtotal or total pancreatectomy. Medical therapy is often required for the patients when surgical therapy is contraindicated or refused by the patient. Medical therapy may also be necessary for the patients with metastatic insulinomas. A calcium antagonist drug verapamil and a new long-acting octapeptide analogue of somatostatin (SMS 201-995 octreotide) have been found to be effective in patients with insulinomas.^{2-5,7,8} In our recent study we concluded that treatment with octreotide resulted in a clear increase in glucose levels by suppressing insulin secretion but diltiazem, a

Table I Plasma glucose (nmol/l) levels during operation

Time (min)	Case 1	Case 2
0 (octreotide)	—	—
60 (operation)	—	—
75	4.2	7.0
90	7.7	13.7
105	20.4	13.1
120	6.8	11.4
135	12.2	10.7
150	5.5	9.4
165	6.4	10.4

calcium-channel blocking drug, was found to be ineffective in contrast to verapamil.⁵

Prevention of hypoglycaemia during the preoperative and operative periods is of primary importance in the anaesthetic management of insulinomas. These patients can go into hypoglycaemic attacks during operation and large volumes of glucose-containing solutions may be required to prevent this complication. Diazoxide is the most commonly used drug for the management of hyperinsulinism. It is a non-diuretic benzothiadiazine derivative that inhibits insulin release by a direct action on beta cells and also by stimulating adrenaline release. The most prominent side effect of diazoxide is fluid retention.⁹ We did not use and made no comparison for diazoxide. Since diazoxide may result in fluid retention, it may be harmful in the patients characterized by volume overload such as our second patient. Our results with octreotide seem to limit the need to administer large fluid volumes. We found no hypoglycaemic values using octreotide administered subcutaneously one hour before surgery.

Octreotide therapy can safely be used before surgery to prevent hypoglycaemia in patients with insulinoma in whom fluid administration may be contraindicated.

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