THE EFFECT OF OCTREOTIDE ON GLUCOSE AND INSULIN LEVELS IN A PATIENT WITH TYPE 2 DIABETES ON GLIBENCLAMIDE

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SUMMARY - We report the case of a 35 year-old woman with recurrent gastrointestinal bleeding in a type 2 diabetic patient well controlled with glibenclamide. After volume resuscitation and transfusion with packed blood cells an infusion of octreotide at 50 mcg/hr was started. It was decided to start a long term octreotide treatment and the potential effect on her glycemic control was studied. A 75 gram oral glucose tolerance test was performed in two consecutive days with and then without octreotide infusion. With octreotide blood glucose was higher and insulin levels were lower. As clinical indications expand, situations will arise where patients with diabetes on sulfonylureas may require octreotide with a conceivable dramatic worsening of glycemic control.

Key-words: type 2 diabetes, sulfonylureas, octreotide, glycemic control, insulin-secretion.

RÉSUMÉ - Effet de l’octroïtide sur la glycémie et l’insulinémie chez un patient diabétique de type 2 sous Glibenciamide.

Nous rapportons l’observation concernant une femme âgée de 35 ans présentant des hémorragies répétées du tractus digestif, diabétique de type 2, bien équilibrée sous glibenciamide. Après traitement par hydratation et transfusion de sang, une perfusion d’octroïtide 50 mcg/heure a été entreprise. Puis un traitement prolongé par octroïtide fut décidé et ses effets potentiels sur le contrôle glycémique préalablement étudiés. Une charge orale en glucose de 75 g a été réalisée deux jours consécutifs, avec et sans perfusion d’octroïtide. Sous octroïtide les glycémies furent plus élevées et les insulinémies plus basses. Dans la mesure où les indications de traitement par octroïtide se développent il est bon de savoir que des sujets diabétiques de type 2 sous sulfamides hypoglycémiants peuvent voir leur contrôle glycémique se détériorer de façon significative lors de l’administration de ce produit.

Mots-clés : diabète de type 2, sulfamides hypoglycémiants, octroïtide, contrôle glycémique, insulinosécrétion.

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Somatostatin and its analogue octreotide decrease splanchnic blood flow and are used for the treatment of variceal bleeding [1-4]. Octreotide is also utilized for the treatment of non-variceal gastrointestinal bleeding [5]. Somatostatin and its analogues inhibit the secretion of insulin from the pancreas, and somatostatin secreting pancreatic tumors have been demonstrated to cause hyperglycemia [6].

Type 2 diabetes is a common disorder. Many patients are treated with sulfonylureas, which stimulate insulin release from the pancreas. Theoretically, octreotide could impair the insulin response to sulfonylureas and worsen glycemic control in these patients, but the literature in this area is sparse. We present an interesting case of a young woman with type 2 diabetes who required treatment with both octreotide and glibenclamide.

A 35-year-old Caucasian woman had a history of recurrent lower gastrointestinal bleeding. In 1995, she underwent a right hemi-colectomy for presumed angiodysplasia. When she developed recurrent bleeding, a subsequent colonoscopy demonstrated extensive colonic varices. Exploratory laparotomy showed extensive small and large bowel involvement that was unamenable to surgical resection. On this occasion she presented to hospital with recurrent bleeding. The patient was diagnosed with type 2 diabetes on admission on the basis of elevated random blood glucose levels and classic symptoms. She was started on glibenclamide and her blood glucose levels were controlled. The patient was volume resuscitated and transfused with packed red blood cells. Due to recurrent bleeding, an infusion of octreotide was started at 50 mcg/hr. Her lower GI bleeding stopped and her hemoglobin stabilized. When the bleeding stopped, the octreotide was stopped. Her bleeding reoccurred but ceased when the octreotide was restarted. This cycle repeated itself twice and it became clear that octreotide was necessary to prevent rebleeding.

It was felt that the patient would benefit from long term octreotide treatment for her recurrent lower GI bleeding but the potential effect on her glycemic control was unclear. In order to assess this, a 75-gram oral glucose tolerance test was performed on two consecutive days. On the first day, octreotide was infused during the test. On the second day, the octreotide infusion was stopped at midnight on the evening prior to the test. On each occasion, the patient’s oral agent (glibenclamide 5 mg) was given at 0700 hours following an overnight fast. A 75-gram glucose load was administered at 0730 hrs. Blood samples were taken at 0, 30, 60, 120, 150 and 180 minutes. Blood glucose levels were analyzed immediately by the glucose oxidase method utilizing a YSI glucose analyzer (Yellow Springs Instruments, Yellow Springs Ohio). Insulin levels were assayed as previously described [7]. Written informed consent was obtained from the patient prior to the performance of the glucose tolerance tests.

Glucose and insulin levels during the oral glucose tolerance tests are shown in Figure 1. It can be seen that glucose levels were higher and insulin levels were lower during the octreotide infusion.

Octreotide has been described as being useful in treating hypoglycemia induced by sulfonylureas [8, 9]. In patients with type 2 diabetes treated with insulin, octreotide did not significantly alter glucose or insulin levels, hepatic glucose production or insulin mediated glucose disposal [10]. To our knowledge, no previous studies have evaluated the effects of octreotide.

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Control Glucose (mmol/L)</th>
<th>Control Insulin (pmol/L)</th>
<th>Octreotide Glucose (mmol/L)</th>
<th>Octreotide Insulin (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.2</td>
<td>209</td>
<td>8.1</td>
<td>264</td>
</tr>
<tr>
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<td>11.4</td>
<td>328</td>
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<td>311</td>
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<td>961</td>
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<td>5.1</td>
<td>2470</td>
<td>6.7</td>
<td>896</td>
</tr>
</tbody>
</table>

Table I. Glucose and insulin values after a 75 gram oral glucose tolerance test. In the control study, the patient was taking her regular hypoglycemic regimen. In the octreotide study, a concurrent infusion of octreotide was being administered.
tide on glucose and insulin levels in patients with diabetes on oral hypoglycemic agents. Our study focuses on a patient on a sulfonylurea in whom octreotide was required. As clinical indications expand, situations will arise where patients with diabetes on sulfonylureas may require octreotide. When octreotide is started in these patients, it is conceivable that glycemic control could dramatically worsen. Conversely, when the octreotide is stopped, hypoglycemia may result from the unopposed sulfonylurea action.

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REFERENCES