Outcomes of patients with diabetes on peritoneal dialysis (PD) are strongly influenced by cardiovascular and other vascular complications, which are directly related to poor glycemic control. These patients are dialyzed with conventional glucose-containing PD solutions, and the glucose that diffuses into the patients’ circulation leads to further risk of poor glycemic control, increasing the risk of vascular complications and death. The central objective for managing patients with diabetes undergoing PD treatment is to develop strategies that reduce complications and improve quality of life through proper glycogenic control and reduction of peripheral insulin resistance.

Key words
Insulin, insulin resistance, type 2 diabetes, oral antidiabetic agents

Introduction
In most dialysis facilities, diabetic patients with end-stage renal disease constitute between 30% and 40% of all patients undergoing peritoneal dialysis (PD). Outcomes of patients with diabetes on PD are strongly influenced by cardiovascular and other vascular complications, which are directly related to poor glycemic control. These patients are dialyzed with conventional glucose-containing PD solutions, and the glucose that diffuses into the patients’ circulation leads to further risk of poor glycemic control, increasing the risk of vascular complications and death.

Besides insulin, methods for proper glycemic control include new antidiabetic agents and various non glucose and biocompatible dialysis solutions. The central objective for managing patients with diabetes undergoing PD treatment is to develop strategies that reduce complications and improve quality of life through proper glycogenic control and reduction of peripheral insulin resistance.

FIGURE 1 Stages in the progression of type 2 diabetes, based on analysis of data from the U.K. Prospective Diabetes Study Group (1). CVD = cardiovascular disease; PVD = peripheral vascular disease.
from the consequent macrovascular complications such as stroke, leg amputation, and coronary artery disease.

At this stage, insulin production from the beta cells of the pancreas increases so that blood sugar levels remain normal (1–4).

**Stage 2: Early diabetes (year 1 to year 5)**

In later years, the pancreatic beta cells become exhausted and insulin secretion declines. Because of reduced secretion of insulin, blood glucose levels start to rise. Blood-sugar or HbA1c measurements remain slightly elevated (“borderline elevation”).

**Stage 3: Clinical diabetes (year 5 and later)**

In later years, secretion of insulin by the beta cells declines further, and blood-sugar levels continue to rise. It is estimated that, after another 5 years, blood-sugar levels remain persistently high (5). Clinical features at this stage include microvascular complications such as retinopathy, nephropathy, and neuropathy. This stage represents the stage of glucose toxicity (2,3).

### Effects of diabetes progression on the patient

The progression from one stage of type 2 diabetes to the next varies in the individual patient depending on environmental and genetic factors. Patients with chronic renal disease develop insulin resistance that improves after dialysis, but complications from glucose toxicity progress if the state of hyperglycemia is not reversed. Patients on PD are at higher risk for such complications because of the use of glucose-containing dialysis solutions (6).

### Management of the diabetic PD patient

Management of the diabetic PD patient should be based on an understanding of the earlier-described staging of diabetes and how it affects that particular patient. Table I summarizes the management approach. In making decisions about treatment options, the focus should be on the stage of the disease, dialysis, and the extra glucose calorie load from dialysis fluids (approximately 300 calories daily).

The goals of treatment are to reduce vascular damage and insulin resistance by using a stepwise approach.

**Table I: Choice of therapy for patients with type 2 diabetes on peritoneal dialysis**

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulin resistance</strong></td>
<td><strong>Early diabetes</strong></td>
<td><strong>Diabetes with hyperglycemia</strong></td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>&gt;6</td>
<td>6–7</td>
</tr>
<tr>
<td>Lipids</td>
<td>High</td>
<td>—</td>
</tr>
<tr>
<td>CRP</td>
<td>High</td>
<td>—</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>Diet</td>
<td>Diet</td>
</tr>
<tr>
<td>Exercise</td>
<td>Exercise</td>
<td>Exercise</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Glyburide (DiaBeta)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Gimeperide (Amaryl)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Risk</td>
<td>Do not use (lactic acidosis if GFR &lt; 20 mL/min)</td>
</tr>
<tr>
<td>Metformin (Glucophage)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>—</td>
<td>Safe [improves insulin resistance (8)]</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Pioglitazone (Actos)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rosiglitazone (Avandia)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Metaglipinide</td>
<td>—</td>
<td>Hypoglycemia, use normal dose</td>
</tr>
<tr>
<td>Repaglinide (Gluconorm)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Insulin</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

— Low dose if needed | Insulin IP or SC |

* Individual patients may need different combinations for best results.

<sup>a</sup> Hoechst Marion Roussel, Frankfurt am Main, Germany.

<sup>b</sup> Aventis Group, Paris, France.

<sup>c</sup> Merck Santé SAS, Lyon, France.

<sup>d</sup> Takeda Chemical Industries, Tokyo, Japan.

<sup>e</sup> GlaxoSmithKline, Brentford, United Kingdom.

<sup>f</sup> Novo Nordisk, Bagsværd, Denmark.

CRP = C-reactive protein; GFR = glomerular filtration rate; CHF = congestive heart failure; IP = intraperitoneally; SC = subcutaneously.
approach to interventions. Diet, exercise, and medications should be used to maintain a standard body weight (body mass index of 25 – 30). Angiotensin converting enzyme inhibitors, angiotensin receptor blockers, anti-lipid drugs, acetylsalicylic acid, and vitamins should be used as standard therapy for control of hypertension, vascular damage, and stroke. Blood sugar should be kept at a euglycemic level (HbA1c around 6% – 7%). Patient education for lifestyle change, diet, and exercise should be the primary strategy for prevention of insulin resistance. The addition of oral antidiabetic agents, particularly thiazolidinediones, can be useful (7–9). Although fear of congestive heart failure has limited use of these drugs in dialysis patients, they are the only agents that may be used in patients with renal failure on dialysis for improvement of peripheral insulin uptake. Thiazolidinediones also improve pancreatic function, reduce lipids, and improve vascular remodeling (9). [Metformin also improves insulin resistance and reduces hepatic glucose production, but lactic acidosis contraindicates its use in dialysis patients (7).]

Insulin should be added to thiazolidinediones in stages 2 and 3. Intraperitoneal (IP) administration of insulin is the best physiologic approach for glycemia control, but that route requires higher doses than subcutaneous administration does (5,10). Patients should be allowed to choose the route of administration, because IP insulin adds extra cost. Hypoglycemia is the main side effect of insulin and sulfonylureas; patient education is therefore required to improve acceptance (1,7).

Table I outlines the drugs currently used, with stepwise choices for the various agents used to help PD patients maintain proper blood sugar control. Insulin and thiazolidinediones remain the mainstay of treatment for patients with diabetes on dialysis.

Finally, proper addition of the non-glucose-based dialysis solutions that are currently becoming available should reduce the glucose calorie load and glucose toxicity, helping to maintain euglycemia in patients on PD (11).

References

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