Mycophenolate mofetil (MMF) therapeutic approach in patients with chronic glomerulonephritis (GN)

To the Editor: In a recent issue of Kidney International, Dr. Levin [1] presented successful treatment of patients with membranoproliferative glomerulonephritis (GN) using mycophenolate mofetil (MMF). We obtained contradictory results using MMF in five patients with resistant nephrotic syndrome (NS) during primary GN. MMF (1 g two times daily) was administered to patients as a second approach medication (Table 1). Before MMF therapy, patients were treated with corticosteroids and cyclophosphamide or cyclosporin. Along with MMF, the patients received hypolipemic treatment, angiotensin-converting enzyme (ACE) inhibitors, and small doses of corticosteroids. In the patients, creatinine clearance was normal and stable over a period of several years before introduction of MMF. Positive response was observed in one patient, while in the other four, even an increase in proteinuria was observed, despite prolongation of the treatment up to 18 months. In the patient with diagnosis of focal segmental glomerulosclerosis (FSGS), a marked rise in proteinuria and a decrease in creatinine clearance was observed, with aggravation of renal insufficiency requiring dialysis a year and a half after discontinuation of therapy. The only MMF-sensitive patient in our study was a female with a 13-year history of renal disease who continued to be in remission one year after the MMF treatment was concluded. Results of our study are, therefore, substantially different from earlier reports [2, 3]. The coexisting major lipid and protein disorders, along with low gammaglobulin concentrations, were likely to contribute to increased risk of infections, which resulted in an increase of proteinuria and resistance to treatment. In light of the above, the use of MMF in treatment of primary GN remains controversial.

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Impact of thyroid dysfunction on serum cystatin C

To the editor: In the May 2003 issue of Kidney International, Fricker et al [1] reported that thyroid dysfunction has an impact on serum cystatin C levels. Cystatin C is an endogenous marker of kidney function that has become more and more popular in clinical practice and is believed to be less variable in production and secretion than creatinine [2]. Moreover, in contrast to endogenous creatinine clearance, assessment of cystatin C does not include urine collections, which provides an advantage in clinical practice for it is easier to perform and excludes pre-analytic sampling errors.

While it was shown that thyroid hormone levels inversely correlate with serum creatinine levels [3], Fricker et al [1] demonstrate in their study that thyroid hormone levels directly correlate with cystatin C levels. Consequently, when considering cystatin C levels, glomerular filtration rate is most likely overestimated in hypothyroidism and underestimated in hyperthyroidism.

Table 1. Characteristics of patients before and after MMF therapy

<table>
<thead>
<tr>
<th>Patient age/gender</th>
<th>Diagnosis/duration of disease years</th>
<th>Proteinuria g/24 hours</th>
<th>Creatinine clearance mL/min</th>
<th>Serum protein g/dL</th>
<th>Serum albumin g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>E.W. 24/M</td>
<td>MGN 3</td>
<td>8.5</td>
<td>9.4</td>
<td>108</td>
<td>101</td>
</tr>
<tr>
<td>B.M. 25/F</td>
<td>FSGS 4</td>
<td>6.2</td>
<td>14</td>
<td>99</td>
<td>50</td>
</tr>
<tr>
<td>M.S. 23/F</td>
<td>MGN 13</td>
<td>5.4</td>
<td>2.0</td>
<td>100</td>
<td>124</td>
</tr>
<tr>
<td>L.W. 28/M</td>
<td>FSGS 16</td>
<td>10</td>
<td>10.8</td>
<td>200</td>
<td>189</td>
</tr>
<tr>
<td>J.K. 19/F</td>
<td>MGN 2</td>
<td>4.7</td>
<td>6.4</td>
<td>83</td>
<td>70</td>
</tr>
</tbody>
</table>

Abbreviations are: MGN, mesangial proliferative glomerulonephritis; MMF, mycophenolate mofetil; FSGS, focal segmental glomerulosclerosis.
In a recent study by our group, rats with severe hypothyroidism showed signs of renal failure such as increased blood urea nitrogen, increased creatinine, and decreased creatinine clearance [4], whereas cystatin C levels were not significantly different between groups (unpublished data). This is particularly interesting since renal dysfunction in euthyroid rats has previously been shown to be associated with markedly increased cystatin C [5]. The lack of cystatin C changes in rats with hypothyroid renal failure underlines the notion of Fricker et al [1] to consider cystatin C with some caution when thyroid dysfunction is present.

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