Effects of Deflazacort Versus Prednisone on Bone Mass, Body Composition, and Lipid Profile: A Randomized, Double Blind Study in Kidney Transplant Patients*

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ABSTRACT
To compare the effects of deflazacort (DEFLA) vs. prednisone (PRED) on bone mineral density (BMD), body composition, and lipids, 24 patients with end-stage renal disease were randomized in a double blind design and followed 78 weeks after kidney transplantation. BMD and body composition were assessed using dual energy x-ray absorptiometry. Seventeen patients completed the study. Glucocorticoid doses, cyclosporine levels, rejection episodes, and drop-out rates were similar in both groups. Lumbar BMD decreased more in PRED than in DEFLA ($P < 0.05$), the difference being particularly marked after 24 weeks ($9.1 \pm 1.8\%$ vs. $3.0 \pm 2.4\%$, respectively). Hip BMD decreased from baseline in both groups ($P < 0.01$), without intergroup differences. Whole body BMD decreased from baseline in PRED ($P < 0.001$), but not in DEFLA. Lean body mass decreased by approximately $2.5\, \text{kg}$ in both groups after 6–12 weeks ($P < 0.001$), then remained stable. Fat mass increased more ($P < 0.01$) in PRED than in DEFLA ($7.1 \pm 1.8\, \text{kg}$ vs. $3.5 \pm 1.4\, \text{kg}$). Larger increases in total cholesterol ($P < 0.03$), low density lipoprotein cholesterol ($P < 0.01$), lipoprotein B2 ($P < 0.03$), and triglycerides ($P = 0.054$) were observed in PRED than in DEFLA.

In conclusion, using DEFLA instead of PRED in kidney transplant patients is associated with decreased loss of total skeleton and lumbar spine BMD, but does not alter bone loss at the upper femur. DEFLA also helps to prevent fat accumulation and worsening of the lipid profile. (J Clin Endocrinol Metab 83: 3795–3802, 1998)

ONE LOSS (1), muscular wasting (2), carbohydrate intolerance (3) and redistribution of total body fat (4) are the price of long term glucocorticotherapy. Recently, we have shown that early after grafting, kidney transplant recipients lose significant amounts of mineral from axial skeleton, with a nadir at 6 months (5) and partial recovery between 6 and 18 months (6) after transplantation. The cumulative dose of prednisone (PRED) was a major determinant of bone loss in these patients. Deflazacort (DEFLA), an oxazoline analog of PRED, has been shown to affect intestinal calcium absorption (7) and urinary excretion of calcium and hydroxyproline (8, 9) much less than the parent substance, at least on a short term basis. Treatment with DEFLA for several months or more also induced less bone loss than other corticosteroids, as assessed by photon absorptiometry (10) or bone histomorphometry (11). However, controlled long term studies using the precise technique of dual energy x-ray absorptiometry (DXA) are lacking to support this concept.

Furthermore, DEFLA has been shown to have fewer side-effects than PRED on glucose and lipid metabolism (12); its use may thus be of interest in transplant recipients, inasmuch as DEFLA appears to have a similar immunosuppressive effect as PRED, e.g. in heart transplant patients (13). However, the effect of DEFLA vs. PRED on body composition, i.e. fat and lean mass in such patients has not been precisely studied to date.


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Study design

Clinical parameters and renal function were monitored twice a week during the first month, on a weekly basis up to month 3, and every 2 weeks thereafter. Complete laboratory assessment (blood and urine) was performed 1, 4, 6, 12, 24, 36, 52, 64, and 78 weeks after KTX. Bone density and body composition were measured at the same visits, except at weeks 4 and 52.

Immunosuppression and concomitant drug therapy

All patients were treated with glucocorticosteroids and cyclosporin A. Azathioprine was added to the regimen in eight patients; in two of them it was given from time of KTX on, and in six patients it was given later (i.e. 2–12 months after KTX).

Oral glucocorticosteroid therapy was given as tablets of 5 and 1 mg PRED or 6 and 1.2 mg DEFLA, following as closely as possible an ideal schedule depicted in Fig. 1. This dose ratio of 1:2:1 had been established in earlier studies (9, 16–18).

Acute graft rejection episodes were treated with iv methylprednisolone (500 mg/day) for a maximum of 6 days. Patients who had received more than six boluses of methylprednisolone (i.e. >3 g) were excluded from the study.

Four patients (one PRED and three DEFLA) received phosphate supplementation for symptomatic hypophosphatemia. Hypertension (n = 16) was treated with β-blockers, calcium channel blockers, and/or angiotensin-converting enzyme inhibitors. Ranitidine was used to prevent peptic ulcer in all patients as long as the daily dose of glucocorticosteroids was above 15 mg prednisone equivalent. One woman (DEFLA) was receiving hormone replacement therapy (HRT; Premarin® 0.625, Wyeth AHP, Schweiz AG, Zug, Switzerland) at the time of enrollment; the treatment was continued throughout the study. Hypercholesterolemia was treated with simvastatin in one patient (DEFLA, treatment started 3 months after KTX) and with fenofibrate in the two patients (one DEFLA and one PRED), who dropped out after 24 weeks.

DXA measurements

DXA (Hologic QDR 1000W) was performed to measure bone mineral density (BMD) at the lumbar spine and proximal femur of the non-dominant leg. In addition, whole body was scanned for assessment of total skeletal BMD and body composition (i.e. lean body mass and fat body mass). Precision error in vitro was 0.4% for BMD, based on daily scanning of an anthropometric phantom supplied by the manufacturer. No drift was seen during the period of investigation. Based on repeated measurements performed at our institution, precision error in vivo is 1% or less for BMD at all sites and for body composition.

Blood and urine collection, biochemistry

Fasting plasma concentrations of calcium, phosphorus, creatinine, glucose, glycosylated hemoglobin; serum concentrations of triglycerides, cholesterol [total, low density lipoprotein (LDL), and high density lipoprotein (HDL)], and apolipoproteins A1 and B2; as well as plasma alkaline phosphatase activity were measured using standard techniques in the central laboratory at our institution. Ionized calcium was measured in whole blood using an ion-selective electrode (Ciba-Corning Diagnostics Corp., Medfield, MA). The serum concentration of intact PTH was measured using an immunoradiometric assay (Allegro, Nichols Institute Diagnostics, San Juan Capistrano, CA). Serum concentrations of 25-hydroxyvitamin D and osteocalcin were measured by RIAs (Nichols Institute Diagnostics).

Fasting urine samples (second morning voided urine) were analyzed for calcium and creatinine by autoanalyzer techniques. Urinary deoxy-pyridinoline was measured by high performance liquid chromatography (19) and expressed as the deoxy-pyridinoline/creatinine ratio.

Twenty-four-hour urine was collected and analyzed for calcium and creatinine by autoanalyzer techniques. Creatinine clearance was calculated and adjusted for 1.73 m².

Data analysis

All values are expressed as the mean ± sem. Changes over time were analyzed with ANOVA for repeated measures with post-hoc t tests using a statistical software package (StatView 4.0 and SuperAnova, Abacus Concepts, Berkeley, CA). Two-way ANOVA was used to judge the time-group interaction. If necessary (as was the case for lumbar BMD), intergroup differences at baseline were corrected using analysis of covariance.

Analysis was performed over 78 weeks for the 17 patients (10 PRED and 7 DEFLA) who completed the study, with additional analysis over 24 weeks for the 19 patients (11 PRED and 8 DEFLA; including the 2 patients who dropped out after 6 months).

Results

Baseline characteristics of the patients (12 women and 7 men) are given in Tables 1 and 2. All parameters were similar between groups, with the exception of lumbar BMD, which was significantly lower in the group treated with PRED than in that given DEFLA.

Rejection episodes occurred in 5 of the 19 patients followed, 3 of them belonging to PRED and 2 to the DEFLA group. Two of them (males) dropped out after week 24: 1 patient (DEFLA) for ESRD and the other (PRED) for having received more than 6 boluses (3 g) of methylprednisolone. Immunosuppressive therapy, including PRED dose, was similar in both groups; based on the equivalence ratio of PRED:DEFLA = 1:1.2, the cumulative oral steroid dose was similar in both groups both after 24 weeks (PRED, 66 ± 6 mg/kg prednisone; DEFLA, 80.4 ± 4.8 mg/kg deflazacort; P = NS; 19 patients) and at the end of the study (PRED, 132 ± 14 mg/kg prednisone; DEFLA, 151.2 mg/kg deflazacort; P = NS; 17 patients). Patients had also received similar doses of iv methylprednisolone after 24 weeks (PRED, 35 ± 4 mg/kg; DEFLA, 27 ± 7 mg/kg; P = NS; n = 19) and at the end of the study (PRED, 33 ± 4 mg/kg; DEFLA, 29 ± 6; P = NS; n = 17). Cyclosporine blood trough levels did not differ significantly at any time point between the groups (data not shown). Azathioprine had been given to 5 of 11 patients in the PRED group vs. 3 of 8 patients in the DEFLA group.

The blood ionized calcium concentration at baseline was above the normal range (1.15–1.30 mmol/L) in 8 patients and below the normal range in 2 patients; the mean value was above the upper normal limit. The plasma phosphate con-
centration was below the normal range (0.74–1.55 mmol/L) in 11 patients and was normal in the remaining patients. The mean value was below the normal range. The intact PTH serum concentration was above the normal range (10–65 pg/mL) in 9 patients and below the normal range in 1 patient; as expected in patients with ESRD, the mean value was above the upper normal limit. The mean daily calcium excretion was below the normal range. No patient had a low serum level of 25-hydroxyvitamin D. Normal values were found for markers of osteoblast activity, i.e. plasma alkaline phosphatase activity and serum osteocalcin concentration. However, mean urinary excretion of deoxypyridinoline, a marker of bone resorption, was slightly above the normal range. Finally, patients had normal serum total and LDL cholesterol, decreased HDL cholesterol and apolipoprotein A1, and slightly elevated triglycerides.

**Bone metabolism**

**Bone density measurements.** Figure 2 depicts BMD changes over time at different skeletal sites for the 17 patients who completed the study.

**Lumbar spine.** Whereas in the PRED group, BMD significantly decreased over time ($P < 0.0001$, by one-way ANOVA for repeated measurements), it did not significantly change in the DEFLA group ($P = \text{NS}$). Intergroup differences were significant ($P < 0.05$) even after correction for baseline intergroup difference using analysis of covariance. At the end of the study, patients treated with PRED had lost $8.0 \pm 2.2\%$ of their initial BMD ($P < 0.01$), whereas patients treated with DEFLA had BMD similar to that measured at baseline ($-1.4 \pm 3.6\%; P = \text{NS vs. baseline}$).

**Upper femur.** At the upper femur, a significant decline in BMD from baseline was observed in both groups ($P < 0.01$, by ANOVA for repeated measurements). There were no significant intergroup differences.

**Total skeleton.** Whole body BMD significantly decreased from baseline in PRED ($P < 0.001$, by ANOVA for repeated measurements), but not in DEFLA ($P = \text{NS}$), patients. After 78 weeks, PRED patients had lost $2.3 \pm 0.8\%$ of their baseline BMD ($P < 0.02$), whereas DEFLA patients had no significant bone loss compared with baseline ($-0.8 \pm 0.1\%; P = \text{NS}$). Intergroup comparison by two-way ANOVA, however, did not reveal significant differences between PRED and DEFLA due to the large SEM combined with the low number of patients per group.

**Biochemical parameters**

Table 2 gives baseline values and changes in the laboratory parameters observed between weeks 1 and 24 as well as week 78.

Creatinine clearance improved slightly to reach a mean value of $62 \pm 4$ mL/min·1.73 m$^2$ at the end of the study. There was a marginal rise in the blood ionized calcium concentration. Serum phosphate concentrations normalized ($1.08 \pm 0.04$ mmol/L), and the mean serum level of intact PTH decreased to the upper normal range ($62 \pm 13$ pg/mL). Neither plasma alkaline phosphatase activity nor urinary excretion of deoxypyridinoline significantly changed over time, whereas the mean osteocalcin serum concentration increased up to the high normal range ($10.1 \pm 1.6$ ng/mL). The mean daily urinary excretion rate of calcium also returned to the normal range ($3.4 \pm 0.4$ mmol/24 h).

For any of these parameters, no difference was found between the groups. Excluding the patient receiving HRT did not influence the results.
Bone parameters at baseline and after 24 and 78 weeks

<table>
<thead>
<tr>
<th></th>
<th>Week 1 (normal range)</th>
<th>Week 24</th>
<th>Δ</th>
<th>Week 78</th>
<th>Δ</th>
<th>P value changes over time</th>
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<td></td>
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<td>Within groups&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Creatinine clearance</td>
<td>(75–127)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>(mL/min/1.73 m²)</td>
<td></td>
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<tr>
<td>PRED (n = 10)</td>
<td>52 ± 4</td>
<td>68 ± 6</td>
<td>+16 ± 6</td>
<td>61 ± 5</td>
<td>+8 ± 5</td>
<td>NS</td>
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<tr>
<td>DEFLA (n = 7)</td>
<td>56 ± 7</td>
<td>57 ± 6</td>
<td>+2 ± 6</td>
<td>64 ± 8</td>
<td>+9 ± 4</td>
<td>NS</td>
</tr>
<tr>
<td>All</td>
<td>54 ± 4</td>
<td>64 ± 4</td>
<td>+10 ± 4</td>
<td>62 ± 4</td>
<td>+8 ± 3</td>
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<td>Ionized calcium (mmol/L)</td>
<td>(1.15–1.30)</td>
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<td>PRED</td>
<td>1.33 ± 0.02</td>
<td>1.35 ± 0.03</td>
<td>+0.02 ± 0.02</td>
<td>1.33 ± 0.04</td>
<td>0 ± 0.03</td>
<td>NS</td>
</tr>
<tr>
<td>DEFLA</td>
<td>1.23 ± 0.05&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.34 ± 0.02</td>
<td>+0.11 ± 0.05</td>
<td>1.29 ± 0.04</td>
<td>+0.06 ± 0.06</td>
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<td>All</td>
<td>1.29 ± 0.03</td>
<td>1.34 ± 0.3</td>
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<td>1.31 ± 0.03</td>
<td>+0.02 ± 0.03</td>
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<td>Phosphorus (mmol/L)</td>
<td>(0.74–1.55)</td>
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<td>PRED</td>
<td>0.68 ± 0.07</td>
<td>0.97 ± 0.08</td>
<td>+0.29 ± 0.09</td>
<td>1.09 ± 0.05</td>
<td>+0.40 ± 0.06</td>
<td>0.01</td>
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<td>DEFLA</td>
<td>0.71 ± 0.12</td>
<td>0.96 ± 0.06</td>
<td>+0.25 ± 0.12</td>
<td>1.07 ± 0.08</td>
<td>+0.37 ± 0.07</td>
<td>0.003</td>
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<tr>
<td>All</td>
<td>0.69 ± 0.06</td>
<td>0.96 ± 0.05</td>
<td>+0.27 ± 0.07</td>
<td>1.08 ± 0.04</td>
<td>+0.39 ± 0.04</td>
<td>&lt;0.0001</td>
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<tr>
<td>Intact PTH (pg/mL)</td>
<td>(10–65)</td>
<td></td>
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<tr>
<td>PRED</td>
<td>105 ± 23</td>
<td>81 ± 25</td>
<td>−2 ± 24</td>
<td>70 ± 21</td>
<td>−33 ± 21</td>
<td>&lt;0.0001</td>
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<tr>
<td>DEFLA</td>
<td>111 ± 35</td>
<td>48 ± 10</td>
<td>−65 ± 25</td>
<td>52 ± 12</td>
<td>−59 ± 34</td>
<td>0.001</td>
</tr>
<tr>
<td>All</td>
<td>106 ± 19</td>
<td>67 ± 16</td>
<td>−39 ± 18</td>
<td>62 ± 13</td>
<td>−44 ± 18</td>
<td>&lt;0.0001</td>
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<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>(36–120)</td>
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<td>PRED</td>
<td>61 ± 8</td>
<td>75 ± 8</td>
<td>+14 ± 6</td>
<td>71 ± 9</td>
<td>+11 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>DEFLA</td>
<td>50 ± 6</td>
<td>60 ± 10</td>
<td>+9 ± 8</td>
<td>64 ± 7</td>
<td>+14 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>All</td>
<td>56 ± 5</td>
<td>68 ± 6</td>
<td>+12 ± 5</td>
<td>68 ± 6</td>
<td>+12 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Osteocalcin (ng/mL)</td>
<td>(1.5–13.6)</td>
<td></td>
<td></td>
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<tr>
<td>PRED</td>
<td>3.9 ± 1.1</td>
<td>7.7 ± 0.9</td>
<td>+3.8 ± 0.7</td>
<td>9.9 ± 2.5</td>
<td>+6.0 ± 2.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DEFLA</td>
<td>2.2 ± 0.5</td>
<td>8.4 ± 0.8</td>
<td>+6.3 ± 1.0</td>
<td>10.3 ± 1.8</td>
<td>+8.1 ± 1.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>All</td>
<td>3.2 ± 0.7</td>
<td>8.0 ± 0.6</td>
<td>+4.8 ± 0.6</td>
<td>10.1 ± 1.6</td>
<td>+6.9 ± 1.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>U-D-pyridinoline/creatinine (nmol/mmol)</td>
<td>(4–21)</td>
<td></td>
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<tr>
<td>PRED</td>
<td>23.3 ± 2.6</td>
<td>26.2 ± 1.9</td>
<td>+2.9 ± 1.4</td>
<td>28.0 ± 4.1</td>
<td>+4.6 ± 3.7</td>
<td>NS</td>
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<tr>
<td>DEFLA</td>
<td>22.5 ± 2.6</td>
<td>21.7 ± 2.6</td>
<td>−0.8 ± 1.7</td>
<td>25.1 ± 4.1</td>
<td>+2.5 ± 4.1</td>
<td>NS</td>
</tr>
<tr>
<td>All</td>
<td>23.0 ± 1.8</td>
<td>24.3 ± 1.6</td>
<td>+1.3 ± 1.2</td>
<td>26.8 ± 2.9</td>
<td>+3.8 ± 2.7</td>
<td>NS</td>
</tr>
<tr>
<td>Urinary 2-h calcium/creatine (mmol/mmol)</td>
<td>(&lt;0.45)</td>
<td></td>
<td></td>
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<tr>
<td>PRED</td>
<td>0.31 ± 0.10</td>
<td>0.50 ± 0.14</td>
<td>+0.19 ± 0.18</td>
<td>0.33 ± 0.09</td>
<td>+0.02 ± 0.13</td>
<td>NS</td>
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<tr>
<td>DEFLA</td>
<td>0.20 ± 0.05</td>
<td>0.39 ± 0.16</td>
<td>+0.19 ± 0.16</td>
<td>0.26 ± 0.08</td>
<td>+0.06 ± 0.11</td>
<td>NS</td>
</tr>
<tr>
<td>All</td>
<td>0.26 ± 0.06</td>
<td>0.46 ± 0.10</td>
<td>+0.19 ± 0.12</td>
<td>0.30 ± 0.06</td>
<td>+0.04 ± 0.09</td>
<td>NS</td>
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<tr>
<td>Urinary 24-h calcium (mmol/24 h)</td>
<td>(2.5–7.5)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PRED</td>
<td>2.0 ± 0.4</td>
<td>3.9 ± 0.7</td>
<td>+1.9 ± 0.7</td>
<td>2.7 ± 0.4</td>
<td>+0.7 ± 0.5</td>
<td>0.004</td>
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<tr>
<td>DEFLA</td>
<td>1.5 ± 0.2</td>
<td>4.5 ± 0.9</td>
<td>+2.9 ± 0.9</td>
<td>4.3 ± 0.9</td>
<td>+2.7 ± 0.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>All</td>
<td>1.8 ± 0.2</td>
<td>4.1 ± 0.5</td>
<td>+2.3 ± 0.6</td>
<td>3.4 ± 0.4</td>
<td>+1.5 ± 0.5</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Follow-up of laboratory parameters in the 17 patients who completed the study. No difference between groups was found when including all 19 patients who completed only the first 24 weeks (data not shown). Values are the mean ± SEM.

<sup>a</sup> By one-way ANOVA for repeated measurements, weeks 1, 4, 6, 12, 24, 36, 52, 64, and 78.

<sup>b</sup> By two-way ANOVA for repeated measurements, weeks 1, 4, 6, 12, 24, 36, 52, 64, and 78.

<sup>c</sup> P = 0.051 vs. PRED (by t-test).

0.001) in both groups, with no significant intergroup difference. There was no correlation between the changes in lean body mass and the changes in urinary creatinine excretion at any time point.

Conversely, fat mass significantly increased in both groups (P < 0.001). However, this increment occurred earlier in the time course and was of greater extent in the PRED compared with the DEFLA group (P < 0.01). At the end of the study, fat mass had increased by 7.1 ± 1.8 kg in the PRED group compared with 3.5 ± 1.4 kg in the DEFLA group.

Lipid and carbohydrate metabolism (Table 1 and Fig. 3). There was no significant difference between the PRED and DEFLA groups at baseline with respect to serum parameters of lipid and carbohydrate metabolism. Serum levels of total, HDL, and LDL cholesterol as well as of lipoproteins A1 and B2 increased significantly (P < 0.001) in both groups. This increase was more marked in the PRED than in the DEFLA group for total cholesterol (P < 0.03), LDL cholesterol (P < 0.01), and lipoprotein B2 (P < 0.03). These results persisted after exclusion of the patient receiving simvastatin (the two patients taking fenofibrate had not completed the study and were therefore excluded from analysis). Serum concentrations of triglycerides tended to increase in the PRED group and decreased slightly in the DEFLA group (P < 0.05). The plasma glucose concentration did not change significantly in either group. However, there was a nonsignificant trend (P = 0.17) for higher blood glucose concentration in the PRED group (6.1 ± 0.6 mmol/L) compared with that in the DEFLA group (5.05 ± 0.22 mmol/L) at month 6. Hemoglobin A1c did not change significantly in either group (data not shown).

Excluding the patient receiving HRT did not influence results for body composition or lipids.
Discussion

The present study shows for the first time that using DEFLA instead of PRED in kidney transplant patients helps to prevent bone loss at the lumbar spine and whole body and leads to lower fat accumulation and a lesser impairment of the lipid profile.

An important issue to be addressed when comparing two glucocorticosteroids is their respective potency. Fewer side-effects may be related to less primary activity. The bioequivalence of DEFLA and PRED has been investigated in various situations. In normal subjects (20), 15 mg DEFLA inhibit T cell reactivity to the same extent as 12.5 mg PRED, but for a longer period of time (based on phytohemagglutinin-induced T cell proliferation in vitro).

Based on the results of seven trials of various design, including double blind cross-over studies, paired patient studies, and between-patient studies involving 160 patients, the potency ratio of DEFLA vs. PRED was estimated by Avioli to be 1.28 (16). In fact, the equivalence ratio of DEFLA/PRED may depend on the disease [i.e. 1.2:1 in rheumatoid arthritis (9), juvenile chronic arthritis (17), and nephrotic syndrome (18); 1.4:1 in asthma (21) and polymyalgia rheumatica (22)]. Few data are available for kidney transplantation. In a study comparing DELFA vs. methylprednisolone using a 1.5:1 ratio (which is equivalent to a 1.2:1 DEFLA/PRED ratio), Elli et al. (23) concluded that there was a more potent immunosuppressive activity of DEFLA with a lower ratio of CD4⁺/CD8⁺ lymphocytes. Taken together, these data support the 1.2:1 potency ratio used in the present study. Indeed, we did not observe any differences in the glomerular filtration rate or the number of graft rejection episodes between the two groups. The actual glucocorticoid dosage was,
in fact, much higher than the preplanned schedule, because physicians adjusted the dose visit after visit according to clinical status and creatinine levels to be on the safe side and to avoid a rejection crisis. Despite this individual dose adjustment, the daily and cumulative doses administered were strictly equivalent in both groups according to the 1.2:1 ratio.

One can argue that the study lacks statistical power to be really conclusive. Due to fewer graft donors than foreseen, the planned sample size of 60 could not be achieved. However, our results for bone density of the PRED group are perfectly consistent with previous studies of kidney transplant patients receiving that drug showing predominant bone loss at lumbar spine and relative bone preservation at limbs (5, 24). Julian et al. (24) found a 6.8% decrease in lumbar BMD 6 months after renal transplantation, with no further loss up to 18 months and a slight increase in the BMD of the radius. In a previous study by our group, patients lost an average of 7% of lumbar BMD and 2% of whole body BMD during the first 5 months after KTX, whereas they did not lose bone mineral at limbs (5). In the present study, lumbar and whole body BMD decreased by 9.1% and 2.3% in PRED-treated patients compared to 3% and 0.8%, respectively, in DEFLA-treated patients. This 6% bone-sparing effect at the lumbar spine would approximately correspond to a reduction by 1.4-fold in the risk of vertebral fractures (25).

A bone-sparing effect of DEFLA at the level of lumbar spine has been described in various clinical situations. In a 1-yr double blind prospective study of patients with the nephrotic syndrome, bone loss induced by PRED at the lumbar spine was 1.9-fold higher (12.5%/yr) than that induced by DEFLA (6.8%) (26). In a randomized double blind prospective study of adult men with newly diagnosed rheumatoid arthritis, patients given DEFLA experienced spinal bone loss at one third the rate of that ob-

![Fig. 3. Changes in serum lipids after kidney transplantation in patients receiving either PRED (rectangles) or DEFLA (filled circles). Statistics were determined by ANOVA for repeated measurement and post-hoc tests (*, P ≤ 0.05 vs. baseline; †, P ≤ 0.05 between groups). ANOVA results: total cholesterol, LDL cholesterol, and lipoprotein B2, changes significant in both groups (P < 0.001), with intergroup differences (P < 0.03–0.01); HDL cholesterol and lipoprotein A1, changes significant in both groups (P < 0.001), with no significant intergroup difference; triglycerides, changes significant in DEFLA (P < 0.05), but not in PRED (P = 0.07), with intergroup difference (P = 0.054).](https://academic.oup.com/jcem/article-abstract/83/11/3795/2865299)
served in the subjects receiving PRED at equivalent dosage (27). Another 12-month study of 22 patients with rheumatoid arthritis, asthma, or sarcoidosis revealed a 10%/yr bone loss during DEFLA vs. 21% during PRED treatment (28). Furthermore, in children with juvenile chronic arthritis, spinal bone growth was greater during DEFLA than during PRED treatment (17).

It has been suggested that DEFLA depresses the osteoblast less than PRED, leading to a smaller decrease in serum osteocalcin levels with this drug (29). Surprisingly, in our patients serum osteocalcin levels increased in both groups despite decreasing PTH levels. This finding can be explained by cyclosporin A cotreatment, which is known to increase bone turnover (30). Other researchers have claimed that some of the bone-sparing effect of DEFLA compared to that of PRED could be explained by a less impaired intestinal calcium absorption by the former (31). The fact that 1) serum ionized calcium significantly increased in the DEFLA but not in the PRED group; 2) the mean intact PTH level showed a trend to a more marked reduction in the former (−57%) compared with the latter (21%) group; and 3) calcitriol tended to increase more in the DEFLA (+200%) than in the PRED (+95%) group suggests better calcium absorption during DEFLA than during PRED treatment.

The lack of statistical significance could be due to the particular condition of renal transplantation that restores 1α-hydroxylase activity, leading to increased calcitriol serum levels (not measured in this study) and calcium absorption.

Fat accumulation is a well known side-effect of glucocorticoid therapy as a consequence of peripheral resistance to insulin with decreased glucose tolerance and increased serum levels of triglycerides. Obviously, the increase in fat mass was less marked in our patients treated with DEFLA (+3 kg) than in those treated with prednisone (+7 kg). As a consequence, triglycerides increased less in the DEFLA-treated patients, although fasting blood glucose and hemoglobin A1C levels were similar in the treatment groups. An additional beneficial effect of DEFLA was found for total cholesterol, LDL cholesterol, and lipoprotein B2. In renal transplant patients, Elli et al. (23) also observed lesser weight gain, better glucose tolerance, and lower increase in serum levels of cholesterol and triglycerides with DEFLA than with methylprednisolone. In another study of 31 heart transplant patients, Belker ME, Massey DM, Vaughan L, et al. 1995 A longterm prospective study of deflazacort, a new synthetic steroid with fewer undesirable side effects, in heart transplant patients. J Heart Lung Transplant. 12:445–449.

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References

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The Third International Strang Cancer Prevention Center Conference
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