The Efficacy of an Initial Prednisone Monotherapy Regimen on PLA2R-associated Idiopathic Membranous Nephropathy

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ABSTRACT

The aim of this study was to evaluate the efficacy and safety of prednisone monotherapy for phospholipase A2 receptor (PLA2R)-associated idiopathic membranous nephropathy (IMN). This was a retrospective cohort study involving 32 patients enrolled between January 2017 and June 2019 at Beijing Friendship Hospital, Capital Medical University, Beijing, China. Seventeen patients received prednisone monotherapy, and 15 received the Ponticelli regimen. The primary outcome was nephrotic syndrome remission at 12th month. The secondary outcomes were the incidence of adverse events and recurrence over the 12-month follow-up. At 12th month, 16/17 patients (94.1%) in the prednisone monotherapy group and 14/15 patients (93.3%) in the Ponticelli regimen group achieved remission (p = 0.19). The adverse events occurred in 9/17 and 9/15 of the patients receiving prednisone monotherapy and the Ponticelli regimen, respectively (p = 0.74). Four and three patients relapsed in the prednisone monotherapy and Ponticelli regimen groups, respectively (p = 0.99). Initial prednisone monotherapy had similar efficacy and safety compared with the Ponticelli regimen for PLA2R-associated IMN.

Key Words: PLA2R-associated idiopathic membranous nephropathy, Ponticelli regimen, Prednisone monotherapy.

were compared by Fisher’s Exact test, and normally distributed
continuous variable data were compared by the t-test. Repeated
measurement data comprised urinary protein and serum
albumin concentrations, and these data were compared by
generalised estimating equations. Kaplan–Meier analysis was
used to estimate remission rates, and the log-rank test was used
to compare the remission rates between the two groups.

A total of 32 patients with IMN were included; 53.1% (17/32)
comprised the prednisone monotherapy group and 46.9%
(15/32) comprised the Ponticelli regimen group. The follow-up
period was 12 months. The demographic data and biochemical
parameters of the patients in the two groups were comparable at
baseline (Table I). Kidney tissue PLA2R antigen was positive for
all patients. Serum anti-PLA2R antibodies were assessed in 25
patients and were detected in 50.0% (5/10) and 53.3% (8/15) of
the patients in the prednisone monotherapy and Ponticelli
regimen groups, respectively (p = 0.99). The therapeutic
regimen was adjusted in seven and one patients in the predni-
sone monotherapy and Ponticelli regimen groups, respectively.

Regarding the primary outcome, nephrotic remission at 12th
month was achieved in 94.1% (16/17) of the patients in the pre-
dnisone monotherapy group and 93.3% (14/15) of the patients in
the Ponticelli regimen group, with no statistical difference in the
cumulative incidence of remission (p = 0.19; log-rank; Figure
1a). The median remission time in both groups was six months.

Table I: Baseline characteristics of the IMN patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Prednisone (n=17)</th>
<th>Ponticelli regimen (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>12/5</td>
<td>11/4</td>
<td>0.99</td>
</tr>
<tr>
<td>Age (year)</td>
<td>51.9±11</td>
<td>54.4±10.7</td>
<td>0.52</td>
</tr>
<tr>
<td>Urinary protein (g/24 hr)</td>
<td>5.4±1.3</td>
<td>6.4±1.8</td>
<td>0.09</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>22.5±3.4</td>
<td>22.1±3.1</td>
<td>0.73</td>
</tr>
<tr>
<td>Serum creatinine (μmol/L)</td>
<td>74.1±8.5</td>
<td>77.3±12.8</td>
<td>0.58</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>8.1±2.3</td>
<td>7.3±3.1</td>
<td>0.40</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>2.0±1.0</td>
<td>2.9±1.3</td>
<td>0.04</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>8 (47.1%)</td>
<td>9 (60.0%)</td>
<td>0.50</td>
</tr>
<tr>
<td>ACEI or ARB – No. (%)</td>
<td>8 (47.3%)</td>
<td>14 (40.0%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Statins – No. (%)</td>
<td>13 (76.5%)</td>
<td>14 (93.3%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Kidney tissue PLA2R antigen positive</td>
<td>17 (100%)</td>
<td>15 (100%)</td>
<td>NA</td>
</tr>
<tr>
<td>Anti-PLA2R – U/mL*</td>
<td>162.4±78.8</td>
<td>107.9±68.2</td>
<td>0.23</td>
</tr>
<tr>
<td>Anti-PLA2R positive – No. (%)</td>
<td>8/15 (53.3%)</td>
<td>5/10 (50%)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Values represent mean ± standard deviations. *The anti-PLA2R titers were calculated only in patients with positive serum anti-PLA2R. †Patients were considered anti-PLA2R-positive if the value was ≥ 20 U per milliliter. ‡By Fisher’s Exact test, ‡by t-test. ACEI: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin receptor blockers; F: Female; IMN: Idiopathic membranous nephropathy; M: Male; PLA2R: Phospholipase A2 receptor.

Figure 1: Probability of nephrotic syndrome remission during the 12-month follow-up and changes in urinary protein or serum albumin levels.

The previous studies showed that Asian patients with IMN responded well to steroids. Consistent with previous studies, it was found that the nephrotic syndrome remission rates in patients receiving prednisone monotherapy were similar to those of patients receiving the Ponticelli regimen. In the present study, the baseline characteristics, especially urinary protein and serum albumin, were well-balanced between the two groups, and these markers were important predictors of clinical outcomes in IMN. The efficacy of the Ponticelli regimen was confirmed in several clinical studies. However, the safety of the Ponticelli regimen remains controversial. In the current study, the incidence of adverse events in the prednisone monotherapy group was similar to that in the Ponticelli regimen group. Notably, the authors did not evaluate reproductive toxicity, which was a conclusive and irreversible side effect of cyclophosphamide. The current study showed that the efficacy and safety of prednisone monotherapy were similar to that of the Ponticelli regimen. Therefore, prednisone monotherapy may be an alternative for PLA2R-associated IMN, especially for patients with fertility requirements.

There were several limitations in this study. First, the sample size was relatively small. Second, it was not possible to periodically monitor serum anti-PLA2R antibodies owing to limitations...
in the hospital laboratory. In conclusion, prednisone monotherapy showed similar efficacy to that with the Ponticelli regimen in patients with PLA2R-associated IMN.

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**ETHICAL APPROVAL:**
This study was approved by the Hospital (2021-P2-269-01).

**CONFLICT OF INTEREST:**
The authors declared no conflict of interest.

**AUTHORS’ CONTRIBUTION:**
YB, JL: Contributed equally to this work.
YB, JL, YD: Performed data collection and manuscript writing.
ZD: Designed and performed the statistical analysis.
WL: Reviewed the manuscript and provided final approval of the manuscript.

**REFERENCES**


