Chlorambucil therapy in children with steroid-resistant nephrotic syndrome

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Chlorambucil (CHL) had been used as treatment for childhood nephrotic syndrome (NS) for more than half a century.\(^1\) It was used mainly in children with steroid sensitive nephrotic syndrome (SSNS) as steroid sparing agent in those with frequent relapsing or steroid dependent course.\(^2\) However, it was observed to result in higher rates of severe side effects and recommended as a second line drug after cyclophosphamide (CYC), which is considered as safer alkylating agent.\(^2\) The alkylating agents have been used for treating steroid resistant nephrotic syndrome (SRNS).\(^3\) However, CYC was used in most of the studies,\(^3\) while CHL was used only rarely.\(^4,5\) Elzouki et al showed in a small study that CHL induced complete or partial remission in patients with SRNS caused by either focal segmental glomerulosclerosis (FSGS) or mesangial proliferative glomerulonephritis (MPGN).\(^4\)

In this retrospective study, we report our results of using CHL in children with SRNS secondary to IgM nephropathy, FSGS or diffuse mesangial hypercellularity (DMH). All patients presented to our unit over 20 months period (from February 2002 until June 2004) and were diagnosed as SRNS were recruited. Steroid resistant nephrotic syndrome was defined as a failure to go into remission after 4 weeks of prednisolone therapy at a dose of 60 mg/m\(^2\)/day, plus 3 intravenous doses of methylprednisolone (600 mg/m\(^2\)/day or 30 mg/kg/day) on alternate days. We had 7 patients with SRNS. All patients were females. The median (range) age at presentation was 4 (2-9) years. All except 2 were Arab in origin. All studied children were primary non-responders to prednisolone and 2 were also resistant to intravenous cyclophosphamide course. All the 7 children were treated with CHL (0.1-0.2 mg/kg/day) for 8-12 weeks. The mean ± SD accumulative dose was 10.1 ± 3.3 (7.0-15.2) mg/kg. All patients were continued on oral prednisolone 40mg/m\(^2\) on alternate days and received enalapril (0.5-1 mg/kg) throughout the CHL therapy. Two patients achieved complete remission after 12 weeks of CHL therapy. One patient remained in remission for 2 years following CHL therapy and one patient had a relapse once after 1.5 years of follow up, which responded to prednisolone promptly. She had been on one year remission. Two patients received CYC of 500 mg/m\(^2\) per month for 6 doses before CHL therapy. The rest of the patients did not respond after 8 weeks of CHL therapy (Table 1). All of them except one were treated subsequently with Cy A. Two patients achieved complete remissions on Cy A while one patient achieved partial remission only. One patient was treated with CyA initially as the histopathology showed FSGS. However, she was treated with CHL when she showed sign of CyA toxicity and achieved

<table>
<thead>
<tr>
<th>Patient’s no.</th>
<th>Age at onset (years)</th>
<th>Sex</th>
<th>Histopathology</th>
<th>Pre-therapy</th>
<th>Duration of therapy (weeks)</th>
<th>Accumulative dose (mg/kg)</th>
<th>Post-therapy</th>
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<td></td>
<td></td>
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<td>S. cr (umol/l)</td>
<td>Urine protein</td>
<td>S. alb (g/l)</td>
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<td>3+</td>
<td>12</td>
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<td>IgM nephropathy</td>
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<tr>
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<td>DMH</td>
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<td>19</td>
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<td>FSGS</td>
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<td>85</td>
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</tbody>
</table>

F - female, IGM - ???, DMH - diffuse mesangial hypercellularity, FSGS - focal segmental glomerulosclerosis, S.alb - serum albumin, S.cr - serum creatinine, -ve = negative

Table 1 - Laboratory data before and after chlorambucil therapy in individual patients.
We conclude that CHL therapy in a total accumulative dose of 15 mg/kg and 12 weeks duration could achieve complete remission in children with SRNS secondary to IgM nephropathy. Further randomized controlled studies are required.

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