Original Article

Ponticelli regimen in idiopathic nephrotic syndrome

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ABSTRACT

Various studies have demonstrated that treatment with methyl prednisolone and chlorambucil could increase the chance of remission of idiopathic nephrotic syndrome (INS) of varied histology in patients who do not respond to the conventional treatment. This study was done to assess the safety and efficacy of methyl prednisolone and chlorambucil regimen in patients with various types of glomerulonephritides which were resistant to the usual conventional immunosuppressive drugs. Thirty nine patients were treated between June 1998 and December 2003 with Ponticelli regimen for six months. Twenty three patients (58.98%) were men and 16 (41.02%) were women. Mean age at the onset of NS was 23.59 ± 1.28 (range 10-51) years. Four patients (10.2%) had minimal change disease (MCD), six patients (15.4%) had membranoproliferative glomerulonephritis (MPGN), two (5.1%) had IgA nephropathy, and 18 patients (46.1%) had focal segmental glomerulosclerosis (FSGS). Eleven patients were excluded from the final analysis. Of the remaining 28 patients, mean baseline proteinuria was 3.31 ± 3.09 g/day. Mean baseline plasma albumin was 2.84 ± 1.002 g/dl and mean baseline serum creatinine was 0.87 ± 0.42 mg/dl. At the end of six months of treatment, mean proteinuria was 1.02 ± 0.85 g/day. Mean plasma albumin was 3.69 ± 0.78 g/day, and mean serum creatinine was 0.85 ± 0.26 mg/dl. Mean followup was 13.21 ± 7.7 times in 18.92 ± 12.58 months. At the end of six months of treatment, seven patients (25%) achieved complete remission (CR), 10 patients (35.71%) partial remission (PR), and 11 patients (39.3%) did not show any response to the therapy. Most of the patients in responder group had FSGS (64.70%), whereas in nonresponder group patients had MPGN and mesangioproliferative glomerulonephritis (MesPGN). Out of 13 FSGS cases five (38.46%) achieved CR, six (46.15%) PR, and only two (15.38%) failed to respond. The incidence of side effects was 39.3%. Responders had more side effects than nonresponders (47 vs 27.3%). Methyl prednisolone and chlorambucil therapy (Ponticelli regimen) is safe and efficacious in achieving remission in significant number of INS patients other than membranous nephropathy, without any serious side effect on short term followup. However, a longer followup is required to demonstrate the sustained efficacy and long-term side effect of this regimen.

Key words: Idiopathic nephrotic syndrome, Ponticelli regimen, prednisolone, chlorambucil

Introduction

There is no standard therapy for patients with frequent relapsing or steroid-dependent nephrotic syndrome (NS) with primary glomerulonephritides (GN).[1] Similarly, the optimal approach to steroid resistant idiopathic nephrotic syndrome (INS) is uncertain. Prolonged or repeated steroid therapy can lead to a variety of serious side effects.[2] Achieving remission is an important goal that predicts an excellent long-term prognosis. For over 30 years cyclophosphomide (CYC) and chlorambucil (Chl) have been used to treat children with relapsing steroid sensitive NS.[3] Seventy five to eighty percent of patients with focal segmental glomerulosclerosis (FSGS) are steroid resistant and majority of them slowly progress to endstage renal disease (ESRD)[4] Ponticelli *et al.*, in a long follow up of a randomized controlled study had concluded that six months course of methyl prednisolone (MP) and Chl can increase remission of protienuria and protect from deterioration of renal function in membranous nephropathy. They also observed similar result with the same treatment protocol in steroid resistant NS with FSGS and frequently relapsing (FR) GN with minimal changes disease (MCD) in various studies.[5] Several studies have demonstrated that treatment with MP and Chl could increase the chance of remission in varied histology in patients who do not respond to the conventional treatment.[1]

We conducted this prospective study to evaluate the safety and efficacy of MP and Chl regimen in patients with various types of GN, who were resistant to the usual immunosuppressive drugs

Original Article

Pattern of biopsy-proven renal disease in a single center of south India: 19 years experience

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ABSTRACT

The prevalence of biopsy-proven glomerulonephritis varies according to the geographic area, socioeconomic condition, race, age, demography and indication of renal biopsy. This study analyzed the distribution of biopsy-proven renal disease (BPRD) and its changing pattern over a period of 19 years from a tertiary care hospital in south India. All the renal biopsies performed from 1990 to 2008 were reviewed retrospectively. Biopsies were evaluated by light microscopy and immunofluorescence microscopy and also special stains when warranted. A total of 1849 biopsies were analyzed. The mean patient age was 32.27 ± 18.38 (range 10-80) years. The male:female ratio was 1.4:1. The most common indications of renal biopsy were nephrotic syndrome (49%), followed by chronic renal failure (13.6%) and rapidly progressive renal failure (12%). Primary glomerulonephritis (PGN) comprised 1278 (69.1%) of the total patients. Among the PGN cases, the most common one was minimal change disease (21.8%), followed by focal segmental glomerulosclerosis [FSGS (15.3%)], membranous glomerulonephritis (10%), chronic glomerulonephritis (9.7%), postinfectious glomerulonephritis (8.1%), mesengioproliferative glomerulonephritis (7.5%), diffuse proliferative glomerulonephritis (6.7%), crescentic glomerulonephritis (6.5%), IgA nephropathy [IgAN (6.3%)], membranoproliferative glomerulonephritis (5.7%), focal proliferative glomerulonephritis (1.6%) and IgM nephropathy (0.5). Secondary glomerular disease (SGN) accounted for 337 (18.2%) of the cases. The most common SGN was lupus nephritis (80.1%), followed by amyloidosis (8%) and diabetic nephropathy (6.5%). Tubulointerstitial disease [124 (6.7%)] and vascular disease [60 (3.2%)] were less common. End-stage changes and miscellaneous disease were found in 37 (2%) and 13 (0.7%) cases, respectively. The incidence of FSGS and IgAN has been increasing since 1999. This study provides descriptive biopsy data and highlights the changing incidence of renal disease which is probably contributed by an increase referral due to increased awareness together with increased manpower and infrastructure.

Key words: Epidemiology, glomerulonephritis, nephropathy, renal biopsy

Introduction

Renal biopsy is a definitive diagnostic test in patients with renal parenchymal disease. Indications of renal biopsy vary from center to center.[1] Renal biopsy is useful for identifying the specific diagnosis, assessing the level of disease activity, and for allowing specific decisions about treatment to be made. The common clinical situations where biopsy is needed are nephrotic syndrome (NS), prolonged acute renal failure (ARF), rapidly progressive renal failure (RPRF), systemic diseases with renal dysfunction, non-nephrotic proteinuria, isolated microscopic hematuria, unexplained chronic renal failure (CRF), renal transplant dysfunction, and familial renal diseases.[2]

Renal biopsy data analysis is essential to study the prevalence of biopsy-proven renal disease (BPRD) and its variation and distribution as per geographic areas, socioeconomic conditions, race, age and indication for renal biopsy, to understand the regional epidemiology of glomerular disease in a particular geographical region. It also improves the understanding of the utility of renal biopsy and acts as a framework for future research into renal parenchymal disease. Unfortunately, we do not have a central biopsy registry in India. Studies on the prevalence of renal disease in India are limited.[3-6] Evidence from different published articles across the world indicates a changing pattern of glomerular disease over the last few decades.[7-21] We have completed 19 years

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Original Article

Nondiabetic kidney disease in type 2 diabetic patients: A single center experience

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ABSTRACT

Nondiabetic renal disease (NDRD) is seen as a cause of proteinuria and renal failure in type 2 diabetes mellitus (DM). The clinical differences between NDRD and diabetic glomerulosclerosis (DGS) are not clear. This study was done to find the spectrum of NDRD in type 2 DM patients and differences in clinical profile between NDRD and DGS patients. Data of patients with type 2 DM who underwent renal biopsy in this institute from 1990 to 2008 were analyzed retrospectively. Patients were categorized as isolated NDRD, NDRD with DGS, and isolated DGS. A total of 75 patients were included. Mean age was 45 ± 10.2 years, male to female ratio was 3.1 : 1, median duration of DM was 12 months (range, 1 year-15 years), proteinuria was 4.2 ± 3.4 g/day, and serum creatinine was 4.3 ± 3.9 mg/dl. Hypertension was observed in 63 (84%) cases and microscopic hematuria in 24 (32%) cases. Nephrotic syndrome (38.7%) was the commonest clinical presentation. Forty-eight (64%) cases had NDRD and 27 (36%) had DGS. The commonest NDRD was minimal change disease (12.5%). Three (6.3%) patients had lupus nephritis. Tubulointerstitial nephritis has been observed in 10.4% patients. No significant differences between NDRD and DGS patients were found except hypertension which was significantly high in the DGS group. Acute kidney injury and nephritic syndrome were not observed in the DGS group. In conclusion, the incidence of biopsy-proven NDRD in type 2 DM in this study was high. Kidney biopsy aided in the detection of NDRD in clinically suspected patients.

Key words: Kidney biopsy, nondiabetic renal disease, type 2 diabetes

Introduction

Proteinuria in diabetic patients is usually interpreted as a clinical manifestation of diabetic nephropathy (DN). However, not all diabetic subjects with proteinuria have DN. Nondiabetic renal disease (NDRD) has been seen to cause proteinuria in diabetic patients. There is a wide variation of prevalence of NDRD. The occurrence of NDRD in type 1 diabetes mellitus (DM) is rare in comparison with those with type 2DM. Although exact incidence of NDRD is not known, frequency varies from 5% to 71% in various studies.[1] It is seen in 26.7% of Asian and 22% of European patients.[2-4] Kidney biopsy is an unbiased method, but is seldom used in proteinuric diabetic patients. Olsen, in a meta-analysis of similar studies, found the frequency of glomerulonephritis (GN) to be between 0 and 66%. These variation is probably due to variable selection criteria and geographical differences.[5] Late age of onset of DM, absence of neuropathy, absence of retinopathy, and presence of other systemic diseases are reported as markers of NDRD in different studies. However, it remains unclear which clinical factors have greater value in the prediction of NDRD. As the reported incidence of NDRD in type 2 DM is high, it is necessary to predict, diagnose, and treat the concurrent glomerular diseases because of the prognostic and therapeutic importance.[6] So far, only few such studies had been published from India. We carried out this study to find the clinical, laboratory, and pathological features of NDRD in type 2 DM patients and also to see any significant differences in clinical profile between the NDRD and DGS groups.

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Materials and Methods

The demographic, clinical, and biochemical data of patients with type 2 DM (defined by the American Diabetes

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Renal Data from Asia-Africa

Spectrum of IgA Nephropathy in a Single Center

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ABSTRACT. Immunoglobulin A (IgA) nephropathy (IgAN) is the most common biopsy-proven primary glomerular disease in the world and a major contributor to the worldwide burden of end-stage renal failure, with a wide geographical variation. To determine the incidence, clinical profile and histological pattern of IgAN in our institute, we reviewed all the patients who had native kidney biopsies with the diagnosis of primary IgAN during the period from 1998 to 2009 in the context of the clinical features. A total of 116 patients with IgAN were finally analyzed; 85 (73%) of the patients were male, the mean age of the patients was 29.2 ± 12.2 (range 10–70) years and the mean duration of disease was 10.4 ± 18.7 months (median: 2 months). Hypertension was present in 74 (63.2%) cases. Gross hematuria was rare. The most common clinical presentation was nephrotic syndrome, followed by chronic renal failure. The mean proteinuria level was 2.5 ± 2.3 g/day (median: 1.7 g/day) and the mean serum creatinine level was 3.04 ± 3.3 mg/dL (median: 1.7 mg/dL). The morphological sub-classification (Haas): Class I was the most common (44.4%), followed by class V (23%). IgA co-deposition with C3 and lambda was the most common finding in the immunofluorescence study. The glomerular filtration rate decreased with advanced histological damage. The incidence of IgAN was 7.5%, which is lower as compared with studies from elsewhere. IgAN in our population had a more severe clinical presentation.

Introduction

Primary immunoglobulin A (IgA) nephropathy (IGAN) is defined as the presence of IgA-dominant glomerular deposition in the absence of systemic or other non-renal diseases. It is the most common biopsy-proven primary glomerular disease in the world.[1,2]

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There is a wide geographical variation existing around the globe, with incidence varying from 2–52%. In some countries such as Japan, China, Singapore, Hong Kong and Australia, the statistics show that nearly half of the biopsy-proven primary glomerular disease is IgAN.[3-7] In the European countries, IgAN accounts for 10–20% of the total kidney biopsies.[8] In the United States, this disease is common in certain areas.[8] The incidence is dependent, to a large extent, on variations in

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Renal Data from Asia-Africa

Pulse Cyclophospamide in Severe Lupus Nephritis: Southern Indian Experience

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ABSTRACT. To evaluate the efficacy and safety of the monthly pulse IV cyclophosphamide (IVC) therapy in patients with severe lupus nephritis, we studied 39 patients of lupus nephritis on IVC therapy between 1998 to 2002. Single monthly cyclophosphamide (0.75-1 g/m^2) was infused intravenously with oral prednisolone (0.5 mg/kg per day) and appropriate hydration. Of the 39 patients 25 (86.2%) patients were females and 4 (13.8%) were males. Six (2%) cases had irregular follow-up and 3 patients had expired during the initial cycles and were excluded from the study. The mean age was 25.6 + 6.72 years (range 10-40 years). The mean duration of the disease from the onset to renal biopsy was 24.2 + 18.5 months. The clinical presentations included nephrotic syndrome (34.5%), acute glomerulonephritis (31.0%), Pyrexia of unknown origin (PUO) (10.3%), and rapidly progressive renal failure (6.7%). Renal insufficiency was present in 47.2% cases. Twenty-two (75.9%) patients had diffuse proliferative glomerulonephritis (class IV), 6 (20.7%) focal proliferative glomerulonephritis (class III), and one (3.4%) class Vd. After a mean follow-up of 15.8 months, out of 29 patients, 13 (44.8%) had achieved complete remission, 7 (24.1%) partial remission and 9 (31.0%) cases did not respond to the therapy. Side effects of the therapy included vomiting and nausea (100%) and hair loss during the first few doses of IVC. In addition, one case had dysfunctional uterine bleeding and two patients had avascular necrosis of femoral head. We conclude that our data indicate that IVC in severe lupus nephritis is effective in Indian patients though longer follow-up is required.

Introduction

Systemic lupus nephritis (SLE) is a multisystemic disease with a wide array of immunological abnormalities.[1] Survival of patients with SLE have improved greatly, but lupus nephritis (LN) remains an important cause of morbidity and mortality.[2] The aims of treating lupus nephritis are to induce and maintain remission thereby reducing the risk of progression to renal failure. Immunosuppressive drugs are more efficacious than prednisolone alone in controlling clinical signs of active nephritis, preventing renal scarring, and reducing the risk of end-

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Original Article

Safety and Efficacy of Everolimus in Chronic Allograft Nephropathy

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ABSTRACT. Chronic allograft nephropathy (CAN) is a major cause of late kidney allograft loss. Everolimus, a novel proliferation signal inhibitor, ameliorates CAN by its antiproliferative or apoptosis-enhancing effects. This study aims to evaluate the safety and efficacy of everolimus in renal transplant recipients with calcineurin inhibitor (CNI) withdrawal either due to CAN or calcineurin inhibitor toxicity (CNIT). A total 21 patients with CAN or CNIT converted from CNI to everolimus were prospectively studied from 2006 to 2009. There were 19 males and two females, with a mean age of 32.9 ± 10.7 years. Eight patients had chronic interstitial nephritis, three had diabetes mellitus, nine had end-stage renal disease and one had focal segmental glomerulosclerosis as native kidney disease. The mean duration of dialysis was 10.7 ± 7 months. 57.2% of the patients had CAN and 42.8% had CNIT. Everolimus was started within six months of post-transplantation in six patients, within 6–12 months in two patients, within 1–2 years in four patients and after more than 2 years in nine patients. The mean dose at first month was 1.25 mg/day, at six month was 1.028 ± 0.3 mg/day and at 12th month was 0.97 ± 0.2 mg/day, with a mean trough level of 6.35 ± 3 ng/dL, 5.18 ± 3 ng/dL and 6.43 ± 1.7 ng/dL, respectively. At the 12th month, serum creatinine declined from 2.07 ± 0.58 mg/dL to 1.65 ± 0.81 mg/dL. The mean calculated glomerular filtration rate improved from 40.85 ± 8.8 mL/min to 56.84 ± 11.4 mL/min. No major side-effects were observed. Everolimus along with mycophenolate mofetil or azathioprine and prednisolone as a maintenance immunosuppressive therapy was found to be effective and safe in patients with CNIs withdrawal either due to CAN or CNIT.

Introduction

Chronic allograft dysfunction, which is also known as interstitial fibrosis/tubular atrophy (IF/TA) or chronic graft failure, is the second major cause of long-term graft failure. It is defined as functional and morphological deterioration of a renal allograft at least three to six months after transplantation.[1,2] The incidence is about 2–3% per year. Despite advances in immunosuppressive therapy for control of acute allograft rejection, the long-term renal transplantation outcome had not significantly improved over the last decade.[3] The causes of chronic allograft nephropathy (CAN) are multifactorial. Calcineurin inhibitors (CNIs) have been a cornerstone of immunosuppression in

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