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Research Article

Overview of Glomerulonephritis Treatment

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Abstract

Glomerulonephritis is inflammation of the glomeruli, which are structures in your kidneys that are made up of tiny blood vessels. Glomerular diseases are an important cause of end stage renal disease. Kidney biopsy is mandatory for diagnosis. Treatment with early diagnosis may stopped or prevent end-stage renal failure. Treatment of glomerulonephritis is regulated by the underlying glomerulonephritis type. Glomerulonephritis treatment options include blood pressure control, protein restriction, immunosuppression, and plasmapheresis. In this article we tried to discuss primer glomerulonephritis (minimal change disease, focal segmental glomerulosclerosis, idiopathic membranous glomerulonephritis, IgA nephropathy, idiopathic membranoproliferative glomerulonephritis, C3 glomerulopathy, pauci immune glomerulonephritis, and antiglomerular basal membrane disease) treatments in the context of literature.

MINIMAL CHANGE DISEASE

As Kidney Disease Improving Global Outcomes (KDIGO) supportive treatment, the treatment of hyperlipidaemia with statins and proteinuria treatment with angiotensin-converting enzyme inhibitör (ACEI) / angiotensin receptor blocker (ARB) in normotensives is not recommended in the first episode. The use of ACEI / ARB can be considered in non-quick remission, frequently recurrent and steroid-dependent patients. Diuretic addition with ACEI or ARB may provide the basis for acute kidney damage [1,2].

According to KDIGO guidelines, corticosteroids (prednisolone 1mg / kg maximum 80mg or 2mg / kg maximum 120mg daily) are recommended as initial treatment for patients with nephrotic syndrome. Corticosteroids are recommended for a minimum of 4 weeks if full remission is provided and a maximum of 16 weeks if complete remission is not provided. Steroid therapy is recommended not to exceed 24 months. Cyclophosphamide or calcineurin inhibitors with frequent relapse and steroid dependence, intolerance or contraindication to corticosteroids, are recommended. If prednisolone, cyclophosphamide, cyclosporine and tacrolimus intolerance are present, mycophenolate mofetil (MMF) may be given [1,3,4]. MMF use has been reported to be effective (about 60%–70% of patients) only in small patient cohorts [5,6]. It has been shown that rituximab is effective in the treatment of patients who are frequently relapsed or steroid-dependent [7,8].

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

In all Focal Segmental Glomerulosclerosis **(**FSGS) patients with subnephrotic proteinuria, immunosuppressive therapy is not recommended. ACEI / ARB and sodium restriction are recommended in all FSGS patients. It is thought that immunosuppressives are not injured in cases with intense glomerulosclerosis and interstitial fibrosis. If there is nephrotic syndrome clinic, corticosteroids (prednisolone daily 1mg / kg maximum 80mg or 2mg / kg daily excess maximum 120mg) and immunosuppressive therapy are recommended. If there is intolerance or contraindication to corticosteroids, alternatively calcineurin inhibitors are recommended. However, for calcineurin use, it is necessary not to have significant renal dysfunction at baseline. The combination of high doses of dexamethasone and MMF is recommended for patients who cannot tolerate cyclosporine. The use of steroids in combination with calcineurin therapy increases complete and partial remission of proteinuria in the treatment of steroid-resistant FSGS. Cyclosporine was effective in treatment but relapse rates were high after drug withdrawal [1,9,10]. Corticosteroids are used in combination with MMF and has been shown to be effective [11,12]. Several case reports have shown that rituximab is successfully used in adult patients with steroid-dependent but non-steroid-resistant FSGS [13-15].

IDIOPATHIC MEMBRANOUS GLOMERULO-NEPHRITIS

KDIGO suggests immunosuppressive treatment in the presence of nephrotic syndrome and any of these. Despite the use of antihypertensive and antiproteinuric treatment for at least 6 months, the proteinuria is always ≥ 4 gr / day, provided severe life-threatening symptoms associated with nephrotic syndrome and glomerular filtration rate (GFR) is not less than 25-30mL / min, it is defined as > 30% increase in serum creatinine in 6-12 months period. Membranous Glomerulonephritis (MNG) spontaneous remission is seen in one-third of the patients. If

the patient has serum creatinine> 3.5 mg / dL or GFR <30 mL / min, in patients with reduced renal size by ultrasonography (<8 cm) or in life-threatening serious infections, immunosuppressive therapy is not recommended. KDIGO recommends monthly steroid and oral cyclophosphamide in initial treatment [1].

If the amount of proteinuria of MGN is ≤ 4 gr/day and renal functions are normal, blood pressure ≤ 125 / 75mmHg, ACEI / ARB, diet, follow-up is recommended and immunosuppressive treatment is not recommended. If the amount of proteinuria is ≥ 4 gr/day and <8 gr/kg and renal functions are normal, blood pressure ≤ 125 / 75mmHg ACEI / ARB, diet, 6/12 months follow-up is recommended. If these patients persistent proteinuria ≥ 4 gr/day in follow-up, corticosteroid + cytotoxic agent or calcineurin inhibitors or rituximab are recommended to patients. If proteinuria is present on ≥ 8 gr/day and/or if renal function is impaired, blood pressure ≤ 125 / 75mmHg ACEI / ARB and diet follow-up are recommended. For persistent proteinuria, ≥ 8gr / day corticosteroid +cytotoxic agent or rituximab or calcineurin inhibitors are recommended. KDIGO recommend that initial therapy consist of a 6-month course of alternating monthly cycles of oral and intravenos corticosteroids (intravenous methylprednisolone 1 gr daily for three doses, then oral methyprednisolone 0.5 mg/kg/d for 27 days), and oral alkylating agents (cyclophosphamide 2 mg / kg / day). It is recommended not to use corticosteroid and MMF monotherapy. In nephrotic syndrome relapses, a remission-induced regimen is recommended. However, if alternate steroid and alkalizing agents are given, the same regimen is recommended only once more. It is recommended that treatment agents be changed in conditions where initial therapy is resistant [1,16-23]. Plasma exchange, intravenous immunoglobulin (IVIG) and rituximab treatment have been shown to be successful in treatment resistant patients [24].

IGA NEPHROPATHY

Current guidelines suggest that patients who have persistent proteinuria ≥ 1 g/day despite a trial of the renin angiotensin aldosterone system blockade of adequate duration and good blood pressure control should be considered candidates for immunosuppressive therapy. KDIGO GFR> 50ml / min and 3-6 months conservative treatment (Supply of active blood pressure with ACEI / ARB) persistent proteinuria ≥ 1gr / day disease 6 months corticosteroid treatment is recommended. If there is no rapid renal function and no crescentic glomerulonephritis, immunosuppressive therapy with GFR <30 ml /min is not recommended. If there is rapidly worsening renal function in KDIGO IgA nephropathy, and if crescentic glomerulonephritis, corticosteroids and cyclophosphamide are recommended. KDIGO does not recommend using MMF [1,25-28]. In the studies conducted, there was no difference between MMF and other immunosuppressive agents in the treatment of IgA nephropathy [29,30]. It was emphasized that despite the treatment with optimal blood pressure control for KDIGO 6 months, persistent proteinuria patients could be given fish oil. It also does not recommend the use of anti-agregan drugs [1].

IDIOPATHIC MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

In patients with non-nephrotic proteinuria and normal or stable kidney function, ACEI or ARB proteinuria and hypertension control are recommended. Immunosuppressive therapy is recommended for patients with nephrotic proteinuria or if there is no renal dysfunction. Albumin infusion is recommended when diuretic, fluid and salt restriction, protein intake of 0.8-1 gr/kg/day protein and high carbohydrate intake are required in oedema treatment. In adults, steroid monotherapy has not been shown to be beneficial in the treatment. Cyclophosphamide or mycophenolate combined with steroids is recommended for these patients. If patients have rapidly progressive renal insufficiency, oral cyclophosphamide or MMF is recommended as a plus steroid followed by oral steroids. Combined dipyridamole and aspirin should be evaluated in the treatment. Also, quite interestingly the benefit of anticoagulant therapy has not been shown. In a previous study conducted, it was shown that combined treatment reduced GFR significantly compared to the control group. Rituximab has been shown to be effective in a small number of cases in studies using it [31-35].

C3 GLOMERULOPATHY

C3 glomerulopathy (C3G) treatment is in the form of nonspecific treatment, immunosuppressive treatments, plasma treatment, and inhibition of complement activation. Nonspecific treatment, blood pressure control (priority agents include ACEI/ARB), reduction of proteinuria and reduction of serum lipid level has beneficial effects on the progression of C3G. Optimal blood pressure control <120 / 80mmHg (ACEI / ARB), lipid control and protein-restricted diet is recommended. If the amount of proteinuria is> 500mg/day despite the supportive treatment, if the renal biopsy finds moderate inflammatory findings or if the renal function is impaired prednisolone or MMF is recommended.

Proteinuria> 2 gr/day for supportive treatment of severe disease, prednisolone and immunosuppressive treatment, increased serum creatinine suggesting risk for progressive disease at onset, if there are signs of severe inflammation during renal biopsy, prednisolone pulse dosing, as well as other anti-cellular immunosuppressive,have had limited success in rapidly progressive disease. Data are insufficient to recommend eculizumab as a first-line agent for the treatment of rapidly [36,37].

PAUCIIMMUNE GLOMERULONEPHRITIS

As KDIGO initial treatment, cyclophosphamide with corticosteroid therapy is recommended. If cyclophosphamide is contraindicated, rituximab is recommended instead. For patients who require dialysis treatment or have rapid serum creatinine increase, plasmapheresis is recommended. Azathioprine is recommended in maintenance treatment, MMF is recommended there are allergies. If you have intolerance to both drugs, then methotrexate recommended. The addition of rituximab to sites of glucocorticoid and cyclophosphamide resistant to induction therapy and IVIG or plasmapheresis is also recommended. If upper respiratory tract disease is present, trimethoprim sulfamethoxazole is recommended [1].

European Vasculitis Society/European League against Rheumatism (EUVAS/EULAR) Group suggests cyclophosphamide or rituximab in addition to corticosteroids in induction therapy. Mesna can be given either orally or intravenously to prevent

bladder toxicity. Methotrexate and MMF may only be used in induction therapy in the absence of an organ or life-threatening conditions. Serum creatinine value is> 500 µmol / L (6.5 mg / dL), the vital organ and life-threatening conditions are suggested to cause disease plasma exchange. Azathioprine or methotrexate is recommended in maintenance treatment. If there is intolerance against them, Leflunomide is recommended. It suggests the use of prophylactic trimethoprim sulfamethoxazole [38-43].

ANTIGLOMERULAR BASAL MEMBRANE DISEASE

In KDIGO initial treatment, glucocorticoid and cyclophosphamide are recommended. Plasmapheresis is recommended in addition to patients with dialysis-dependent and pulmonary haemorrhage, who have the crescent of adequate renal biopsy. In the case of anti glomerular basal membrane disease, maintenance treatment is not recommended. As prophylaxis, co-trimoxazole antifungal (nystatin) proton pump inhibitors, or h2 antogonis, calcium and vitamin D are recommended. For immunoadsorption autoimmune diseases, it is an alternative treatment for circulating autoantibodies. This treatment is used for anti-glomerular basal membrane disease [1,44-47].

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