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Review Article

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Introducing the general management of glomerular disease from a pediatric perspective based on the updated KDIGO guidelines

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In 2021, a new chapter on the general management of glomerulonephritis (GN) was added to the Kidney Disease: Improving Global Outcomes (KDIGO). It emphasizes the importance of early general management of GN for improving long-term kidney outcomes and prognosis. The chapter introduces the management of glomerular diseases in 18 subchapters. Here, kidney biopsy for the diagnosis and evaluation of kidney function and the management of complications, such as hypertension, infection, and thrombosis, are presented. Moreover, the adverse effects of glucocorticoids and immunosuppressive therapy, which are commonly used drugs for glomerular disease, are mentioned, and a guideline for drug selection is presented. Each subtheme focused on items reflecting the interpretation of the "practice points" of the expert working group are introduced. In this review of the general treatment for GN in the KDIGO guidelines, excluding pregnancy and reproductive health, we focused on and compared various references pertaining to pediatric GN management.

Keywords: Adult; Child; Glomerulonephritis; Guideline

Introduction

The guidelines for Kidney Disease: Improving Global Outcomes (KDIGO) were updated in 2021, with detailed discussions on 10 diseases based on the general principles for managing glomerular disease [1]. The KDIGO presents high-quality treatment guidelines for adults and children by conducting a rigorous evidence-based review. However, pediatric recommendations are limited [1] due to lack of randomized controlled trials (RCTs) in children and the small number of patients studied. Nevertheless, these guidelines are crucial as they help minimize the discrepancies in treatment policies between adolescents and adults. Moreover, the KDIGO glomerular disease guidelines have an advantage over other recommendations because they are applicable to both children and adults, and specify the differences in treatment and the latest findings for children.

This review summarizes the general principles for managing glomerular diseases (first chapter of the KDIGO 2021 glomerular disease guidelines), focuses on practical points, and examines the contents of pediatric glomerular disease management. Additionally, we reviewed the guidelines for each disease and added comparisons from various references to highlight the differences in adult management. However, pregnancy and reproductive health in women with glomerular disease were

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excluded from subsection 1.15.

Kidney biopsy

Kidney biopsy remains the gold standard for diagnosing glomerular diseases. However, several methods have been developed for diagnosing glomerular diseases. For example, genetic testing can be used to diagnose Fabry disease and Alport syndrome, and familial focal and segmental glomerulosclerosis can be diagnosed in families with well-characterized mutations. Additionally, antineutrophil cytoplasmic antibody-associated vasculitis can be treated without diagnostic confirmation from biopsy [1]. A kidney biopsy is performed for diagnostic purposes for determining treatment options and predicting prognosis. Unlike adult nephrotic syndrome, pediatric steroid-sensitive nephrotic syndrome (SSNS) in patients aged <12 years or post-infectious glomerulonephritis is conventionally treated without biopsy because the clinical features are sufficient for diagnosis [1]. If nephrotic syndrome is accompanied by hematuria or decreased kidney function, if it occurs in patients aged <1 year or >12 years, or if there is no response to steroid treatment, idiopathic nephrotic syndrome should not be considered, and biopsy should be performed to determine the cause.

To ensure the adequacy of diagnosis, at least 8–10 glomeruli were obtained via kidney biopsy [1]. Kidney biopsy in children is an invasive procedure; therefore, appropriate specimens must be obtained using this minimally invasive procedure. Typically, two to three biopsy cores are obtained. Minimal trials are acceptable, as the number of glomeruli per core is reportedly higher at a younger age [2]. The most common complication of biopsy in children is perirenal hematoma, which occurs in approximately 37% [2], and the incidence of hemorrhage requiring transfusion is 0.6% to 2.0% [2,3]. Low estimated glomerular filtration rate (eGFR; <30 mL/min/1.73 m^2) was an independent risk factor for major complications [3]; thus, care must be taken during biopsy for such patients.

Repeat biopsies may be performed when evaluation of disease progression or a change in the treatment plan is required. Repeat biopsies were performed in the following cases [1]: (1) when the decrease in kidney function cannot be explained despite considering the natural course; (2) to consider whether treatment should be changed; (3) to evaluate whether a change in clinical or laboratory parameters occurs in the same diagnosis (e.g., class switching in lupus nephritis); (4) to evaluate the chronicity and activity, and to determine need for alteration of treatment (maintenance/strengthening/ tapering of treatment); or (5) to define a "point of no return/therapeutic futility."

Assessment of kidney function

Proteinuria and GFR

Evaluation of kidney function is important for diagnosis, prognostic evaluation, and determination of future treatment plans. Therefore, proteinuria and eGFR must be assessed [1]. Proteinuria is assessed using 24-hour urine collection, and evaluation of 24-hour urine collection is recommended whenever the medication dose is adjusted, a decision is made to administer or discontinue it, or if the clinical status changes. The definition for 24-hour proteinuria classifications in children is as follows [4]: normal ≤4 mg/m^2/hr, proteinuria 4–40 mg/m^2/hr, and nephrotic-range proteinuria >40 mg/m^2/hr.

Since 24-hour urine collection in children can be inconvenient, especially in infants prior to toilet training, and can be overestimated in orthostatic proteinuria, the first morning urine protein-to-creatinine ratio (UPCR) was used. The 24-hour proteinuria and first morning UPCR show a high correlation [5]. The results of morning UPCR in children are interpreted as follows: UPCR >200 mg/g (>500 mg/g for children aged 6–24 months) is defined as proteinuria [6], and first morning UPCR performed at a urine specific gravity >1.015 of 200 mg/g or higher is defined as fixed proteinuria [4]. Persistent proteinuria is associated with poor prognosis. Regardless of the underlying disease, the target for first morning UPCR is to achieve a normal level of <200 mg/g or <8 mg/m^2/hr in 24-hour urine [1].

Evaluation using eGFR is easier than measuring GFR. The Cockcroft-Gault, Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations are eGFR formulas used for adults, whereas the Schwartz equation and its modifications are widely used for children. The equation for chronic kidney disease (CKD) in patients aged <25 years (CKiD U25 eGFR equation), applicable to both young adults and adolescents in the transitional state, was recently developed [7]. In addition to the Schwartz equation, the full age spectrum (FAS) equation can be applied as an eGFR formula in children [8,9]. The FAS equation is applicable to all ages over 2 years and has the advantage of less discrepancy in the transition state. The GFR value from the FAS equation was not inferior to that from the Schwartz-creatinine equation [8].

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Evaluation of hematuria

Hematuria is an important sign of glomerular disease and is present in approximately 50% to 80% of patients [1]. Urine sediments for erythrocyte morphology, red blood cell (RBC) casts, and the presence of acanthocytes are characteristic markers of glomerular disease [10,11] and should therefore be examined. RBC casts in urine or acanthocytes with >5% urine RBCs indicate inflammatory glomerular disease [1]. The magnitude and persistence of hematuria can predict long-term outcomes in many glomerular diseases, particularly immunoglobulin A nephritis or vasculitis, and is thought to be a prognostic marker [1]; thus, regular follow-up is important for all glomerular diseases.

Management of complications of glomerular disease

Complications caused by glomerular disease may result from the clinical presentation rather than from a specific histological problem. Morbidity and mortality can be improved by addressing metabolic problems and thrombotic events while managing edema, proteinuria, and blood pressure (BP) [1].

Control of edema

Edema may be due to the development of proteinuria or a decrease in GFR. The mechanisms that explain the occurrence of nephrotic edema are as follows [12,13]: (1) Underfill theory: as the serum albumin level decreases with nephrotic-range proteinuria, the total extracellular fluid volume increases; however, the plasma volume decreases as oncotic pressure decreases. In these cases, BP is normal or decreased, and the renin-angiotensin-aldosterone system is activated [14]. (2) Overfill theory: primarily, sodium and fluid retention occur in the distal renal tubule and collecting duct; this mechanism increases the circulating volume, resulting in edema [12].

Salt restriction may be necessary to manage edema in nephrotic syndrome. A salt restriction of 2 g/day is recommended for adults [1]. For salt restriction in children, recommendations such as <2 mEq/kg/day to 1–2 g of salt per day, to a no added salt diet were suggested [15]. However, to date, no recommendations for sodium intake according to a child's age, weight, or sex have been put forth [15].

Loop diuretics should be considered as first-line therapy for edema [1]. It removes sodium and fluid by inhibiting the Na^+-K^+-$2Cl^-$ cotransporter on the apical surface of the thick ascending limb in the loop of Henle. Loop diuretics decrease the reabsorption of sodium in the renal tubule by 20% to 30% [13]. However, the effect of diuretics on nephrotic syndrome is limited, which is caused by an increase in the volume of distribution due to hypoalbuminemia and the urinary excretion of protein-binding drugs [1]. Because the urine output is dose-dependent on loop diuretics, if the initial dose is ineffective, the dose can be increased. Loop diuretics dose for infants and children is 1–4 mg/kg/day [12]. When high-dose loop diuretics are rapidly administered, caution should be exercised to avoid ototoxic complications such as hearing loss and tinnitus. If the response to oral administration is insufficient, the intravenous route may be changed. Gastrointestinal absorption of diuretics is not effective in severe nephrotic syndrome due to intestinal wall edema; therefore, intravenous diuretics may be necessary to provoke effectiveness [1].

Combination therapies, such as loop diuretics, thiazide, and aldosterone antagonists, are more effective for refractory edema than loop diuretic monotherapy alone is. Combination therapy with loop diuretics and thiazide increases urine output by more than 50% compared with loop diuretic monotherapy [12]. Thiazide removes sodium and chloride from the body by inhibiting the Na-Cl cotransporter in the distal renal tubule [12]. In nephrotic syndrome, sodium resorption increases in the distal renal tubule; therefore, thiazide is effective against loop diuretic-resistant nephrotic edema [12].

The addition of potassium-sparing diuretics such as amiloride and spironolactone can reduce potassium loss, and the addition of acetazolamide can improve metabolic alkalosis [1]. When diuretics are ineffective in treating edema accompanied by hypoalbuminemia, the addition of albumin improves intravascular volume depletion and blood osmolarity and increases the elimination of sodium and body fluid [1,12]; its clinical effect is greater in children [1]. If treatment-refractory edema persists, consider dialysis to avoid organ damage, such as pulmonary edema and heart failure.

Control of hypertension and proteinuria

Controlling BP and reducing proteinuria are important for the kidney prognosis [1]. Management of hypertension reduces the risk of cardiovascular disease and kidney function deterioration [1]. Implementing lifestyle modifications, such as appropriate salt intake, weight normalization, and regular exercise, is important for controlling hypertension. In glomerular disease patients, target BP should be lower than that of the general pop-

ulation, especially in children, which aim for ≤50th percentile of the BP distribution according to age, sex, and height.

Decreased proteinuria reduces glomerular hypertension and podocyte damage. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) inhibit angiotensin II, reducing intraglomerular pressure and hyperfiltration [16,17]. It results in reducing BP and proteinuria, slows the progression of kidney disease, and improves cardiovascular outcomes [16]. ACE inhibitors or ARBs can reduce proteinuria by 40% to 50% in a dose dependent manner [1]. An increase in creatinine levels may occur as an adverse effect of the drug owing to a decrease in intraglomerular pressure. Regular monitoring of the GFR and electrolyte levels is necessary because of ACE inhibitors or ARB-induced hemodynamic changes in the kidneys. ACE inhibitors or ARBs should be discontinued if the serum creatinine level increases by >30% from baseline [18]. In addition, ACE inhibitors or ARBs should be discontinued when there is a risk of kidney insult, such as dehydration, because adverse effects can be amplified. Evidence of differences in the therapeutic effects of ACE inhibitors and ARBs are limited. Additionally, it is unclear whether ACE inhibitor and ARB combination therapies are more efficacious. Combination therapy may be used in young adults without diabetes or cardiovascular diseases; however, its benefits and safety remain unclear [1]. In children, the anti-proteinuric effect and slowing of CKD progression with combination therapy are limited, and the results of related studies are inconsistent; therefore, a larger study is needed to obtain accurate results [19]. Mineralocorticoid receptor antagonists may be an alternative treatment option for patients with ACE inhibitor/ARB intolerance. When mineralocorticoid receptor antagonist was administered to patients with CKD who received ACE inhibitors or ARBs, proteinuria was reduced by 15% to 54% and BP was reduced by 40% [20]. However, a decrease in GFR was found in 25% of the RCTs, and one out of eight RCTs reported hyperkalemic events; therefore, the routine addition of mineralocorticoid receptor antagonist (spironolactone) to patients with CKD is not recommended [20].

Management of hyperlipidemia

Hyperlipidemia in glomerular diseases can result from diet, genetic predisposition, nephrotic syndrome, or medication-induced complications [1]. Common risk factors for hyperlipidemia include family history, obesity, diabetes, hypertension, prior cardiovascular disease, persistent proteinuria, and decreased kidney function [1]. The management of hyperlipidemia followed the guidelines for the general population. Lifestyle modifications, such as a heart-health diet, increased physical activity, weight reduction, and smoking cessation, are important and should be considered as first-line treatments, especially for children and adolescents [1]. Additional medications should be considered for hyperlipidemia caused by nephrotic syndrome or other glomerular diseases that cannot be controlled with lifestyle modifications alone. The most commonly used medication is statin [1]. Statins, which are 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, have been shown to decrease the risk of atherosclerotic cardiovascular events in adult patients with CKD in several clinical trials. The kidney-protective effects of statins have not been established [1]; however, some data suggest that statins reduce microalbuminuria, proteinuria, and all-cause mortality in non-end stage kidney disease patients [1,21]. In children aged >8 years, statins can be initiated based on family history, extremely elevated low-density lipoprotein (LDL) cholesterol, or lipoprotein(a) [1]. According to the 2013 KDIGO clinical guidelines for lipid management in CKD, statin administration is not recommended for children aged <10 years because of limited data [22]. The lowest dose can be administered to prevent cardiovascular events in children aged ≥10 years with severely elevated LDL cholesterol levels. In addition, owing to safety and efficacy issues, multidrug regimens are not recommended [22]. If patients have intolerable dyslipidemia with statins or a high risk of atherosclerotic cardiovascular events, consider non-statin therapies such as bile acid sequestrants, fibrates, nicotinic acid, ezetimibe, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors and lipid apheresis. Bile acid sequestrants ezetimibe and PCSK9 inhibitors have been approved for the treatment of pediatric patients [23]. Bile acid sequestrants bind to bile acid, removing it from the enterohepatic circulation, upregulating the LDL receptor, and increased LDL cholesterol clearance [23]. Ezetimibe lowers LDL cholesterol levels by inhibiting intestinal and biliary cholesterol absorption [24], and PCSK9 inhibitors lower serum LDL cholesterol levels by inhibiting PCSK9, which degrades LDL receptors on the surface of live cells [25].

Hypercoagulability and thrombosis

Glomerulonephritis with severe proteinuria is associated with a high risk of thrombotic events. These mechanisms include hyperviscosity due to decreased intravascular volume after

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hypoalbuminemia, urinary excretion of antithrombotic factors, and imbalance in the hepatic synthesis of pro-thrombotic factors [26]. Many thromboembolic events occur within 6 months of the first diagnosis [1]. The incidence of venous thrombosis is higher than that of arterial thrombosis, with deep vein and renal vein thrombosis being the most common. Pulmonary embolism can occur asymptomatically; therefore, caution should be exercised.

Thrombogenic risk factors include [1]: (1) the pathology of membranous nephropathy, the degree of proteinuria, and serum albumin levels (<2.5 g/dL); and (2) additional risk factors include a genetic predisposition to thrombosis, positive antiphospholipid antibodies, immobility, obesity, malignancy, pregnancy, and surgery. When thrombotic events such as venous thrombosis, pulmonary embolism, and nonvalvular atrial fibrillation occur in nephrotic syndrome, they are treated with a full-dose anticoagulant for 6 to 12 months or till the duration of nephrotic syndrome [1]. Intravenous heparin, followed by bridging with warfarin, is preferred, with a target international normalized ratio is 2–3 [1]. Because of fluctuations in serum albumin levels in nephrotic syndrome, the international normalized ratio should be monitored frequently. Direct oral anticoagulants have not been systematically studied in nephrotic patients for the prophylaxis or treatment of thrombosis [1]. When thromboembolism occurs in children, enoxaparin and heparin are administered for acute management and the treatment is changed to warfarin for long-term maintenance. The safety and effectiveness of direct oral anticoagulants in children has not yet been proven; therefore, traditional drugs have been maintained.

Patients at a high risk of thrombosis can be administered unfractionated heparin or low-molecular-weight heparin as a prophylactic anticoagulant [1]. Prophylactic anticoagulation therapy in children is limited and requires careful consideration. Non-pharmacological preventive measures, such as ambulation, compression stockings, and adequate hydration, should first be performed in high-risk patients (e.g., central venous catheter insertion, infection, and thrombophilia) [27]. Prophylactic anticoagulation therapy requires consultation with a hematologist. Relative or absolute contraindications to prophylactic anticoagulation are as follows [1]: (1) patient preference/ability to adhere; (2) bleeding diathesis; (3) central nervous system lesion prone to hemorrhage; (4) genetic mutations influencing warfarin metabolism/efficacy; (5) frailty; or (6) prior gastrointestinal bleeding.

Risk of infection

Patients with glomerular diseases are vulnerable to bacterial infections because of the reduced levels of immunological factors due to proteinuria, dilution of defense factors due to edema, and long-term immunosuppressant use [28,29]. In particular, they are vulnerable to encapsulated bacterial infections owing to the loss of circulating antibodies, and spontaneous bacterial peritonitis caused by *Streptococcus pneumoniae* may occur in the presence of generalized edema and ascites [28]. In cases of repeated infections, intravenous immunoglobulin was administered when the serum immunoglobulin G level was <600 mg/dL [1]. In cases of immunosuppressant treatment, a screening test for infection was performed before drug administration. Appropriate screening is dependent on exposure, which may be unique to particular geographic regions and/or occupations [1]. Serological tests for syphilis, human immunodeficiency virus, and hepatitis B and C are common indicators of underlying glomerular disease. The serological results are related to glomerular disease, and treatment should be considered either preceding or concomitant with immunosuppressants, which can aggravate infectious diseases. Latent tuberculosis, which is common in many populations, should be screened for and treated concomitantly with immunosuppression. Helminth *Strongyloides stercoralis* infections should be screened and treated in at risk individuals before the initiation of immunosuppression, especially with glucocorticoids.

If the infection is confirmed, treatment is initiated, and depending on the severity of the disease, immunosuppressive therapy is initiated. Owing to the high risk of invasive pneumococcal infection in patients with glomerular disease, vaccination against pneumococcus and influenza viruses should be administered. Exposure to the varicella zoster virus can progress to a life-threatening course, especially in children. If a patient is exposed to the varicella zoster virus, zoster immunoglobulin should be administered, and antiviral medication should be added if symptoms occur [1]. Patients receiving regular complement antagonists (e.g., eculizumab) are vulnerable to meningococcal infections. Therefore, vaccination and administration of prophylactic antibiotics against meningococci are essential. A live vaccine is contraindicated in patients receiving immunosuppressive medication; live vaccine administration should be delayed until the dose of steroids (prednisone) is <20 mg/day or 1 to 3 months after the discontinuation of immunosuppressive medication [1]. In SSNS, vaccination, especially

varicella zoster vaccination, should be administered as soon as possible after the first remission. Vaccination of family members living together is important to reduce infections in immunocompromised children. Therefore, pneumococcal and annual influenza vaccinations should be administered. However, when family members are vaccinated with live vaccines, patients should avoid contact with gastrointestinal, urinary, and respiratory secretions for 3 to 6 weeks after vaccination. Prophylactic administration of trimethoprim/sulfamethoxazole can prevent *Pneumocystis* infection when immunosuppressants, such as high-dose prednisone or rituximab are administered.

Outcome measure

If glomerular disease is treated appropriately, the disease progression is halted or slowed down. Proteinuria and GFR are used to evaluate the kidney outcomes. A decrease of 30% or more in proteinuria or albuminuria is an indicator that progression to kidney failure has been prevented, and a decrease in renal function by 40% or more compared with the baseline GFR for 2 to 3 years can be a surrogate marker for progression to kidney failure [1]. Patients should also continue treatment to prevent non-kidney complications.

"Point of no return" means a situation in the natural history of a chronic glomerular disease where severe loss of kidney function (eGFR <20–30 mL/min/1.73 m^2), it is accompanied by extensive and irreversible kidney injury (primarily interstitial fibrosis and tubular atrophy, and/or bilateral renal atrophy) such that any therapeutic strategy being tested cannot reasonably be expected to alter the natural history of progressive deterioration in kidney function (therapeutic futility) [1]. Even patients who have reached the "point of no return" need persistent treatment to avoid non-kidney complications, such as cardiovascular diseases [1].

Administration of glucocorticoid and immunosuppressive therapy

Drugs that treat glomerular diseases should effectively prevent disease progression, while minimizing adverse effects. As the prescription and treatment effects of each drug are mentioned in the guidelines for each disease, this review explains the adverse effects of these drugs.

Glucocorticoid

Glucocorticoids are the main line of treatment for management of several glomerular diseases, particularly pediatric nephrotic syndrome. Nephrotic syndrome is classified according to the initial steroid response, better steroid response, and better prognosis. The well-known side effects of glucocorticoids include physical changes, such as weight gain, body shape changes, acne, growth retardation, and metabolic complications, such as hyperglycemia, diabetes mellitus, and hypertension. Intermittent treatment with high-dose glucocorticoids is unrelated to bone mineral content deficits in pediatric SSNS [30]; however, growth retardation and bone density loss may occur with long-term administration of glucocorticoids. Therefore, bisphosphonates and vitamin D should be administered to prevent these adverse effects. Hence, it is important to administer as few steroids as possible. Steroids are functional growth hormone antagonists that interfere with growth hormone excretion [31]. Growth can be improved by administering growth hormone [31].

Prophylactic antibiotics should be considered to prevent infections caused by long-term steroid administration. Additionally, H2 receptor antagonists and proton pump inhibitors can prevent gastrointestinal complications. However, proton pump inhibitors can cause hypersensitivity to immune reactions, leading to acute interstitial nephritis or acute kidney injury [32,33].

Calcineurin inhibitors

Calcineurin inhibitors reduce T-cell activation and stabilize the actin skeleton of podocyte [28]. It is the primary immunosuppressive treatment for steroid-resistant or dependent nephrotic syndrome. Nephrotoxicity is the best-known side effect of calcineurin inhibitors, although it is uncommon at low trough levels [1]. The risk factors for tubular interstitial lesions include the use of cyclosporine for >24 months and heavy proteinuria for >30 days during cyclosporine use [1]. Other metabolic side effects include as follows [1]: (1) hair growth and gingival hyperplasia (cyclosporine); (2) hypertension and hyperlipidemia (cyclosporine>tacrolimus); or (3) diabetes mellitus and tremor (tacrolimus>cyclosporine).

Cyclophosphamide

Cyclophosphamide depletes immune competent cells by adding an alkyl group to DNA. It also reduces the steroid requirement and risk of relapse in nephrotic syndrome [28,34]. Cyclo-

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phosphamide can cause renal toxicity; thus, dose modification is required depending on kidney function. In addition, monitoring of marrow suppression is required, and the drug should not be used for more than 6 months. Oral hydration is sufficient to reduce bladder toxicity and sodium-2-mercaptoethane sulfonate should be considered when administering high-dose cyclophosphamide. Caution should be exercised when administering a high dose, as it increases the risk of cancer, including bladder cancer and infertility.

Rituximab

Rituximab is a monoclonal antibody against CD20 found in B cell [28]. Rituximab binding to CD20 causes rapid depletion of B cell populations and is effective in steroid-dependent or steroid-resistant nephrotic syndrome, recurrent focal segmental glomerulosclerosis and membranous nephropathy [35]. Rituximab can cause severe complications, such as anaphylaxis due to infusion reactions and hypogammaglobulinemia due to repeated administration. One study has reported a decrease in serum immunoglobulin G levels and an increase in the risk of infection after rituximab administration [36].

Dietary management in glomerular disease

For dietary control in patients with glomerular disease, a reduction in sodium intake helps to reduce BP and edema in patients with nephrotic syndrome. In adults, reducing protein intake based on kidney function is recommended [1]; however, restricting protein intake is inappropriate for growing children. A low-protein diet in children with CKD resulted in significantly low height and growth rates [37], and did not limit the progression of CKD [38]. For optimal growth in children, supplying protein up to the upper normal limit of the age/sex-suggested dietary intake is recommended in CKD stages 2–5. In end stage kidney disease, supplying protein rather than the suggested dietary intake by reflecting the amount of protein exiting from dialysis is recommended [39]. In patients with pediatric nephrotic syndrome, urine protein levels usually decrease within 2 weeks after the start of steroid therapy; therefore, the amount of protein intake is based on the nutrient requirement for healthy children of the same age, considering both the likelihood of progression to kidney failure and their growth [12].

In reduced GFR, calorie restriction with a body mass index higher than ideal is recommended to facilitate weight loss and prevent cardiovascular and kidney complications [1]. Patients with elevated serum cholesterol who are at risk of cardiovascular complications should follow a healthy diet, and fats should be restricted to < 30% of total calories, with saturated fats <10% [1]. In children with nephrotic syndrome, in whom dietary protein is not restricted, there is no need to consume a higher number of calories for their age [12]. Some patients receiving steroid therapy may gain weight, and adequate calorie intake is necessary to prevent obesity [12].

Goals of glomerular disease treatment, post-transplant glomerular disease

The overall goals of treatment of glomerular disease are lasting remission [1]. A complete remission is more desirable, but a partial remission may sufficient [1]. Treatment choice should take into account avoiding or minimizing the treatment-related adverse events [1]. Therapeutic drugs are selected on the basis of their risks and benefits. The treatment plan should consider the patients' convenience or quality of life. As most cases of glomerular diseases, except for minimal change disease, can recur after kidney transplantation [1], the risk of recurrence should be evaluated before and after transplantation, and donor selection and post-transplantation management should be determined. Despite the risk of recurrence after transplantation, transplantation is the best option for patients with kidney failure [1].

Conclusion

Studying glomerular diseases in children is difficult because of the low incidence, limited access, vulnerability, and difficulty in treatment as compared to those in adults. Nevertheless, the prognoses of glomerular diseases in children are a critical factor in determining their current quality of life and lifetime prognosis. Therefore, early detection, appropriate treatment initiation, and standardized treatment protocols are essential. Further focused research and developments are necessary for understanding and managing pediatric glomerular diseases.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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Author contributions

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