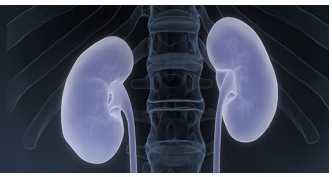
BETTER EDUCATION ON

GLOMERULONEPHRITIS:

IMPROVING KNOWLEDGE OF IgA NEPHROPATHY



1. Overview

Glomerular disease represents an important health, social, and economic issue, especially among children, teenagers, and young adults, as it is one of the leading causes of kidney failure, accounting for 20% to 25% of all cases of end-stage kidney disease (ESKD). IgA nephropathy (IgAN) is the most common form of primary glomerular disease worldwide, with a global incidence among adults estimated to be at least 2.5/100,000 per year. IgAN is defined by the deposition of immune complexes formed by IgA antibodies in the mesangium of the glomeruli. These complexes cause glomerular injuries and inflammation, which can eventually reduce kidney function. The risk of progression to ESKD requiring hemodialysis within 20 to 25 years of diagnosis is approximately 20% to 30%.

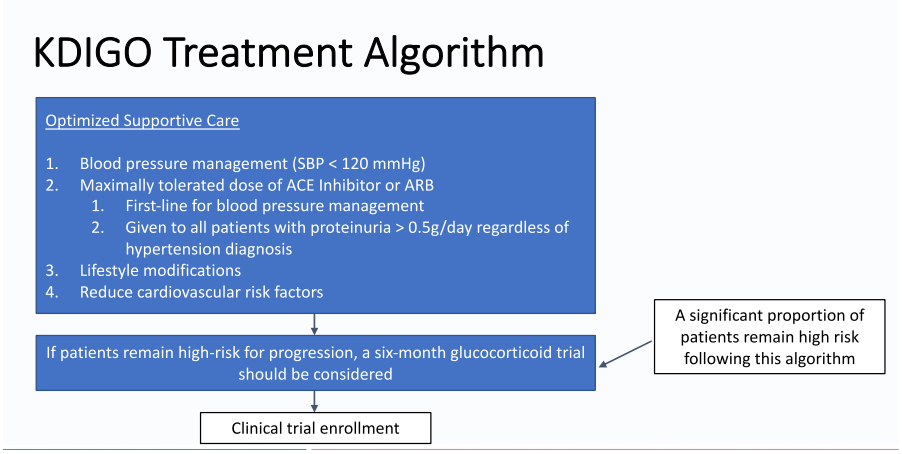
2. Diagnosis of IgAN

Given the characteristic deposition of IgA antibodies in the mesangium of the glomeruli, diagnosis occurs via kidney biopsy using immunofluorescence. Histopathological features (mesangial proliferation, endocapillary proliferation, segmental scarring, and tubular atrophy) have been used to predict long-term outcomes of the disease. Notably, no validated biomarker is available for diagnosis. MEST-C and the International IgAN Prediction Tool are used to risk stratify patients.

3. Proteinuria as a Treatment Target

Proteinuria represents a key risk factor for the progression of IgAN (as well as all chronic kidney diseases). Kidney survival after 10 years is significantly worse in patients with proteinuria >1 gram per day compared to patients with proteinuria <1 gram per day. The National Kidney Foundation, US Food and Drug Administration, and European Medicines Agency identified that early change in albuminuria fulfilled the criteria for use as a surrogate end point in clinical trials for CKD. Consequently, proteinuria has become commonly used as a primary outcome in IgAN trials.

4. Clinical Management of IgAN



Treatment of patients with IgAN mainly consists of supportive care. According to the Kidney Disease: Improving Global Outcomes (KDIGO) 2021 Guideline for the Management of Glomerular Diseases, the main approach for patients with IgAN should include optimal blood pressure control and reduction of cardiovascular risk factors through lifestyle modifications, including salt restriction, weight normalization, regular exercise, and smoking cessation. In addition, proteinuria should be treated with renin-angiotensin system inhibitors such as angiotensin-converting enzyme inhibitor (ACEi) or angiotensin-receptor blocker (ARB). In patients with persistent proteinuria despite supportive care, corticosteroid therapy can be used, but adverse events are a limitation. For patients where lifestyle modifications and steroids do not slow progression, dialysis and/or kidney transplantation is generally required.

5. Emerging Therapies

Targeted-release formulation-budesonide received FDA approval recently to reduce proteinuria in adults with primary immunoglobulin A nephropathy at risk for rapid disease progression. Other classes of therapies that target one or more pathophysiologic mechanisms, and also intended to reduce proteinuria, are in clinical development. These include endothelin receptor antagonists, complement activation inhibitors, B cell activation inhibitors, and A proliferation-inducing ligand (APRIL). Atrasentan, iptacopan, narsolimab, and sparsentan have all entered phase 3 trials.