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The Comprehensive Effectiveness of the Treatment of Chronic Kidney Disease by Tacrolimus: A review

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Abstract

Chronic kidney disease refers to kidney structure and dysfunction due to various causes, and the history of kidney damage is greater than three months. At present, the treatment of chronic kidney disease is treated with immunosuppressants, and tacrolimus as a new immunosuppressant, it has achieved good results in the treatment of Chronic kidney disease. This paper summarizes the pharmacological effects and clinical efficacy of the treatment of chronic kidney disease in the treatment of tacrolimus, with a view to providing reference for rational clinical use. By consulting the relevant literature, the important pharmacological effects and efficacy of Kermos, drug interactions and adverse reactions are summarized and summarized, and the existing research is reviewed. Tacrolimus in the field of Chronic kidney disease treatment is widely used in clinical applications, clear its pharmacological effects and efficacy, drug interactions, adverse reactions, can provide reference for clinical safety and rational use.

Keywords

Tacrolimus; Chronic Kidney Disease; Immunosuppressant.

1. Introduction

Chronic kidney disease(CKD) is chronic kidney structure and dysfunction caused by various reasons (history of kidney damage is more than 3 months).Its pathogenesis includes excessive activation of immune cells, imbalance of cytokines, and obstacles to the production of apoptotic cells and immune complexes. Currently, immunosuppressive agents are generally used to treat glomerular diseases. Tacrolimus (TAC) is a powerful macrolide immunosuppressant and a new type of immunosuppressant. It is clinically used to promote nerve regeneration and atopic dermatitis, and prevent transplant rejection of solid organs. The treatment of autoimmune diseases such as rheumatoid arthritis is a kind of drugs with good curative effect, low incidence of side effects and no renal toxicity. Its main pharmacological mechanism is to form a complex with the K506 binding protein in lymphocytes, thereby interfering with calmodulin-dependent signaling pathways and inhibiting the release of inflammatory response factors such as IL-2, IL-4 and IL-8 by T cells. At the same time, it inhibits the proliferation of T cells and the corresponding proliferation of B cells, exerting an immunosuppressive effect. TAC can also intervene in the maturation of dendritic cells and their antigen-presenting function, play an indirect immune regulatory role, induce T cell incompetence, Treg cell production, etc., thereby inducing immune tolerance, enabling the treatment of chronic diseases. In recent years, the use of tacrolimus to treat chronic kidney disease has achieved good results. This article analyzes the comprehensive effectiveness of tacrolimus in the treatment of chronic kidney disease through domestic and foreign research.

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2. The Application of Tacrolimus in Chronic Kidney Disease

2.1 Primary Membranous Nephropathy (Idiopathic Membranous Nephropathy, IMN)

The pathological manifestation of IMN is the deposition of immune complexes under the epithelial cells of the glomerular basement membrane accompanied by diffuse thickening of the glomerular basement membrane.Glucocorticoid alone is generally not effective for IMN, and tacrolimus combined with glucocorticoid can be used to treat membranous nephropathy. In a domestic study of short-term and long-term observation of IMN patients with nephrotic syndrome, 20 patients were divided into 10 short-term treatment groups and 10 long-term treatment groups, and treated with hormones combined with TAC, short-term treatments The treatment is 6 months, and the long-term treatment is 24 months.The results showed that 5 patients in the short-course treatment group had complete remission, 4 had partial remission, and 1 patient had no effect. After it was over, it was found again that there were 6 cases of recurrence. In the long-term treatment group,6 patients had complete remission, 3 had partial remission, 1 was ineffective, and at the end of the treatment course, there was no recurrence.Through this study, it can be proved that the treatment of IMN by TAC is effective, and the long course of treatment can effectively alleviate the condition, and the recurrence rate is low [1]. In summary, the treatment of IMN with TAC has a faster effect.In recent years, many documents have shown that the clinical efficacy of TAC combined with hormones in the treatment of membranous nephropathy is more obvious than other pathological types of chronic kidney disease, and tacrolimus has more advantages in the treatment of IMN[2-3].

2.2 Chronic Graft Nephropathy (Chronic Graft Nephropathy, CAN)

Chronic allograft nephropathy has chronic rejection of the transplanted kidney.Tacrolimus is a strong calneurinase inhibitor that can effectively inhibit lymphocyte activation and prevent early acute rejection. In a study by Southern Medical University, 59 patients who received cadaveric kidney transplantation and all received an immunosuppressive regimen based on cyclosporine A, and divided them into two groups, namely, CAN with chronic rejection Group and CAN without chronic rejection group. When the pathology confirmed that all patients had CAN, immediately stop cyclosporine A and switch to an immunosuppressive regimen based on tacolimus combined with mycophenolate mofetil. The starting dose of tacolimus was 0.08 mg/(kg·d), the target blood concentration of the drug is 5-8 μg/L, and the fixed dose of mycophenolate mofetil is 1.0 g/d, twice a day, and the drug dose is adjusted according to the patient's own condition and the side effects of the drug. After 6 months, it was found that the serum creatinine, total cholesterol, triacylglycerol, low-density lipoprotein and 24-hour proteinuria of patients in the CAN with chronic rejection group and the CAN without chronic rejection group were significantly lower than those before the conversion. Obviously, and the glomerular filtration rate of the two groups has been significantly increased. In the CAN with chronic rejection group, 20 patients improved;in the CAN without chronic rejection group,9 patients improved. After testing, the effective rates of the two groups were 64.5% and 32.1%, respectively. Compared with the pre-conversion, the incidence of hypertension and hyperlipidemia of the patients decreased significantly[4]. Therefore,tacolimus combined with mycophenolate mofetil-based immunosuppressive program can significantly improve renal transplantation function in CAN patients, especially for patients with CAN with chronic rejection.

2.3 Systemic Lupus Erythematosus (SLEN)

SLEN is an autoimmune disease with multiple organs, multiple system damages and a variety of immunological abnormalities.The clinical symptoms are characterized by facial erythema, fatigue, alopecia, joint pain, skin rash, Raynaud's phenomenon and so on. In a study, 86 elderly SLEN patients were divided into tacrolimus + immunoadsorption therapy group (tacrolimus group) and cyclophosphamide + immunoadsorption therapy group (cyclophosphamide group), with 43 cases in each group. Observe the treatment effect of the two groups of patients and detect the changes of inflammatory response factors and immune function indexes. Results After treatment,there were 32 patients in complete remission and 8 patients in partial remission in the tacrolimus group, respectively.

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The overall efficiency was higher than that of the cyclophosphamide group,and the adverse reaction rate of the tacrolimus group was also lower than that of the cyclophosphamide group[5].In summary, tacrolimus combined with immunoadsorption method has a good clinical effect on elderly lupus nephritis, and can significantly improve the body's inflammatory response and immune function.

2.4 Diabetic Nephropathy (DN)

Diabetic nephropathy is a common complication of diabetic patients with microvascular disease, leading to glomerular sclerosis and decreased glomerular filtration rate [6].As a new type of immunosuppressant, tacrolimus also has a certain effect on diabetic nephropathy. Studies have shown that [7], because tacrolimus has a certain inhibitory effect on immunosuppressive agents, it has a certain inhibitory effect on the activity of cytoplasmic phosphatase calcineurin.It can inhibit renal interstitial fibrosis and renal interstitial fibrosis by blocking TGF-β receptors.Irbesartan can reduce vascular resistance and improve renal vascular endothelial damage.Tacrolimus combined with irbesartan has a synergistic effect.And it can improve kidney function, delay kidney injury,and promote the recovery of kidney function without increasing adverse drug reactions.

2.5 Henoch-schonlein Purpura Nephritis (Henoch-schonlein Purpura Nephritis)

Henoch-Schonlein purpura is mainly due to the effects of certain drugs, allergies and pathogen infections,which cause IgG or IgA-type circulating immune complexes to be generated in the body, thereby invading capillaries and small arteries of the skin or other organs.According to research, it is known that compound glycyrrhizin injection has a significant therapeutic effect on allergic purpura. Through the research of Taihe Hospital in Shiyan City, compound glycyrrhizin injection combined with tacrolimus capsules has a good clinical effect in the treatment of Henoch-Schonlein purpura nephritis,which can significantly improve the renal function and immune function of patients, and reduce the pain of children. Obvious adverse reactions have certain clinical application value [8].

2.6 Chronic Graft Nephropathy (Chronic Graft Nephropathy, CAN)

CAN is considered to be a kidney transplant failure that occurred 3 months after the operation, based on the lack of diagnosis of acute rejection, drug poisoning, etc.It is mainly manifested as a slow increase in blood creatinine, an increase in proteinuria and gradually worsening hypertension drugs [9]. Tacrolimus, as a calmodulin inhibitor, is the most important drug for anti-rejection therapy after solid organ transplantation. It is clinically proven that tacrolimus can effectively prevent the rejection of allografts and improve the survival rate of patients and kidneys in the short term after transplantation. However, tacrolimus is nephrotoxic and can lead to the loss of function of the transplanted kidney. At present, there is no effective means to prevent and treat calmodulin inhibitor nephrotoxicity.Reducing or withdrawing calcineurin inhibitors early after transplantation may be a better choice to prevent calcineurin inhibitor nephrotoxicity [10].

3. Comparison of Tacrolimus and Immunosuppressive Therapy for Chronic Kidney Disease

3.1 Cyclophosphamide

In the treatment of SLEN, cyclophosphamide combined with immunoadsorption method has the effect of inhibiting the inflammatory response of the elderly patients with SLEN,and can improve their immune resistance,but its side effects arestillobvious.It has many aspects such as bone marrow suppression, infection, liver toxicity, etc. Adverse side effects, and the overall adverse reaction rate is as high as 30.23%, higher than the tacrolimus group, and tacrolimus can quickly relieve proteinuria, and the remission rate is better than cyclophosphamide.

3.2 Cyclosporine

Tacrolimus and cyclosporine are both strong calneurin inhibitors.The long-term clinical application of cyclosporine is limited due to adverse reactions such as high blood pressure, hyperlipidemia, atherosclerotic disease and viral infection caused by cyclosporine. According to research, tacrolimus

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is 10-100 times stronger than cyclosporin A in inhibiting lymphocyte activity in vitro. In the treatment of chronic renal allograft nephropathy, it is safer and more effective to switch to tacrolimus treatment, which can improve lipids.Metabolism of qualitative heterogeneity can effectively improve the function of the transplanted kidney and delay the progress of chronic renal allograft dysfunction[11].

4. Conclusion

Tacrolimus is an effective method for the treatment of various chronic kidney diseases, and its efficacy has been clinically confirmed in many aspects. Tacrolimus has high safety, good clinical effects, and easy tolerable side effects. It has a good application prospect and is worthy of further research and popularization.But at the same time, tacrolimus also has problems such as narrow treatment window, large individual differences, drug concentration, easy tolerability of side effects and susceptibility to multiple factors. In this case,,the dose is reduced or stopped in time, it can prevent permanent nerve damage. Clinically, it is necessary to use evidence-based evidence based on existing evidence, and more prospective, multi-center, randomized controlled clinical trials are still needed for research and verification in the future.

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