Research Progress of Drug Therapy for Systemic Lupus Erythematosus

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Abstract. Systemic lupus erythematosus (SLE) is a complex disease with variable presentations, course and prognosis. The incidence varies worldwide, and the current global prevalence of SLE is approximately 10 cases per 2.41 million. [1] Among all these patients, women who are in their childbearing age make up most of the population. This kind of autoimmune inflammation disease decrease the quality of their life. Due to heterogeneity and the incomprehension of exact mechanism of SLE, though we have already developed different types of drug: Hydroxychloroquine, Glucocorticoids, Immunosuppressive (IS) drugs and Biological agents, and multi-drug combination is used in clinical treatment to improve long-term patient outcome, SLE is still very easy to relapse which increases organ damage and leads to poor disease prognosis. Drugs nowadays still treat the symptoms but not the root cause. SLE is a manifestation of the imbalance of various factors in the body. Correcting only the partial imbalance can only delay the damage to body. More precise disease assessment scale, updated detection technology, new therapeutic targets, and new biomarkers are in need.

Keywords: Systemic lupus erythematosus · Drug therapy · Non-drug treatment · Specific manifestations

1 Introduction

The distinct features of SLE is multisystem immune-mediated damage [2]. SLE involves the dysfunction of immune system and cell. Infection, lupus encephalopathy and lupus nephritis are common reasons which rank the top three of the cause of death. Genetic differences, living environment, and hormone, multiple factors have impact on the cause. The prevalence of SLE has been computed to be 30–50 per100 000. There are disparities in SLE's rates among gender and race. Women, especially in childbearing age, are more likely to gain SLE than men do [3]. Black people, Asian and Hispanic's age of onset is earlier than Caucasian, and their clinical symptoms of SLE and the damage to organs is more sever, the progress of illness is more active and these three races face higher mortality than Caucasian. Although SLE is the life threating kind of illness, good prognosis is shown with the development of treatments.

Due to the increase in the number of diagnosed mild cases and rising survival rate, the incidence and prevalence of SLE is going up [4]. The improved patients' outcomes

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owe to the new therapy. Earlier diagnosis and better management of specific organ manifestations and complications, particularly those related to lupus nephritis, have also benefited patients [5].

2 Existing Problems

During the treatment, steroid preparations and immunosuppressant can both compromises the immune system. Patients are susceptible to infection and the infection aggravate the disease itself.

Various presentation and course are presented in SLE. Its diverse manifestations limited to partial body part is in rare cases, but it had led a few physicians specifically look for indication of serological autoimmunity and that has the order reversed clinically [6]. Lacking appropriate biomarkers that can precisely indicate the occur of SLE before the symptoms have appeared might result in missing the easy-to-treat stage and missing the good opportunity to remove infected tree.

3 Goals of Treatment

SLE is an incurable disease. Completely remission is rarely seen. The ultimate goal for patients in SLE is to control their disease condition and to improve their life quality of patients. It is worth noting that the overall health-related quality of life for patients with SLE keeps going down [7].

Higher disease activity in early onset will increase the risk of organ damage and death. Early diagnosis and solutions are conducive to controlling disease activity and improving the prognosis of patients. Completely remission (absence of clinical activity with no use of GC and IS drugs) is rarely seen. The patient should follow the doctor's advice through the whole treatment. Doctors, pharmacists and patients work together to achieve better outcome.

4 Treatment of SLE

The common clinical feature in SLE patients is Recurrence. It might lead to bad organ damage and poor prognosis, and it is also the sign of disease activity. Low age of onset, persistent clinical disease activity and serological activity are the high risk factors of recurrence. The patients often have to be adjusted to prevent and lessen recurrence after achieving disease remission or recurrence reducing. For the adverse reactions of hormones increasing as the dose increase and to avoid the risk caused by insufficient or misuse of drugs, clinicians use the lowest dose required to control the disease.

For long-term improvement of patient outcomes, the whole treatment should direct at symptoms' and signs' remission, minimizing drug side effects, and improving the life quality.

Therapy should aim at least partial remission by 6–12 months. However, complete renal injury takes longer time, basically twelve to twenty-four months. Preventing the flares counts in the SLE treatment. Most doctors acknowledge that flares are measurable increase in disease activity though it is devoid of generally accepted definition currently [6].

4.1 Hydroxychloroquine

Hydroxychloroquine attenuates inflammatory injury by inhibiting cellular immune activation and response. Evidence reveal that there are multiple advantageous effects for using HCQ in people with SLE and hydroxychloroquine is generally recommended to patients. However, it is common in clinical treatment to find out bad adherence with HCQ.

Because of the long terminal elimination half-life, doctors use blood HCQ concentrations to check patients' compliance [8]. Low or even undetectable blood HCQ concentrations suggest the possibility that SLE patient had not followed the instructions of doctors for quite a long time. The most frequent method to monitor blood concentrations is by HPLC. Risk of toxicity isn't high if patients take doses under 5 mg/kg body weight base on the evidence, therefore daily dose should be under this value.

4.2 Glucocorticoids

Glucocorticoids are a class of corticosteroids. GCs can control inflammation, release symptoms, slow the disease degeneration. Only appropriate dosage does no harm to body instead of too high or too low. Irreversible organ damage should be taken into consideration when it comes to long-term GC therapy, so the daily doses should not exceed 7.5mg/day, converted to prednisone dosage [14].

4.3 Immunosuppressive (IS) Drugs

Immunosuppressant are recommended for SLE patients with poor efficacy of hormone combined with HCQ, or patients who cannot adjust the dose of hormone below the relatively safe dose; For patients with organ involvement, immunosuppressant should be added to the initial treatment. The use of immunosuppressant can reduce the cumulative use of hormones and prevent disease recurrence [9].

4.4 Biological Agents

It is proved that B-cell targeting agents have helpful effects in SLE. Belimumab should be taken into consideration in extra renal disease that with inadequate control to first-line medication. Patients who has persistent disease may benefit from biological agents [6].

4.5 Vitamin D

Vitamin D is closely related to sunlight, it is also called "sunshine vitamin", which relates to the increase calcium and phosphorus in blood concentration, and is conducive to the formation of new bone and calcification. However, Vitamin D is in balance with ultraviolet light. The patients are always protected from light. Vitamin D deficiency subsequent to the avoidance of sunshine because sunlight is inversely related to disease activity. Therefore, vitamin D supplement is needed for patients.

5 Non-drug Treatment

5.1 Protect Skin from the Sun

Ultraviolet radiation is recognized as a trigger of SLE. The exposure of both UVB and UVA generate adverse circumstances to patients of systemic lupus erythematosus. UVB mainly cause epidermal damage while UVA cause deep dermal damage including blood vessels, cells and collagen fibres. Sunlight exposure is able to lead to disease course to non-ultraviolet radiation areas, and in few cases, it can decrease organ injury. Because the patients have strong photosensitivity, it is necessary to avoid the sun. Do not go out when the ultraviolet ray is strong to prevent the disease from getting worse. High-efficiency sunscreen is recommended for use in situation when sunlight is unavoidable [10].

5.2 Avoid Light-Sensitive Food

This disease is inherently sensitive to light. If patients eat more food with strong light sensitivity, the disease will become more serious. So it is better to eat less or no rape, fig, celery and other food with increased light sensitivity.

5.3 Prevention of Osteoporosis

Vitamin D is closely related to calcium and phosphorus in blood. Vitamin D deficiency may be caused by the sun protection measures. It is important to get Vitamin D supplement for patients with SLE.

5.4 Exercise and Physical Therapy

Exercise and physical therapy, including coordinated training to quit smoking, reduce coffee and alcohol intake, quit smoking, and increase protein intake. If you adhere to a healthy lifestyle behaviour that can be changed, the risk of developing SLE (a disease that has established important evidence of genetic involvement) may be reduced by nearly 50% [16].

5.5 Psychological Support

Systemic lupus erythematosus is a chronic disease that affects the social and mental health of the body. It is well known that the quality of life (QOL) and psychological status of patients with systemic lupus erythematosus (SLE) are severely impaired. There are three outcome measures to correlate patients with SLE, namely disease activity, damage, and life quality. A good mental state is conducive to the recovery of the disease, it's necessary to give patients environmental support. Also, the health status of relatives may have an impact on SLE patients. In view of the role that family members should play in the supportive treatment of these patients, the poor QOL and psychological state of their relatives may aggravate the mental state of patients. Therefore, health care providers should emphasize that nursing units include patients and their families.

6 Specific Manifestations

6.1 Lupus Nephritis (LN)

Lupus nephritis is one of the most severe organ manifestations of the autoimmune disease SLE. Most patients with SLE who develop LN do so within 5 years of an SLE diagnosis and, in many cases, LN is the presenting manifestation resulting in the diagnosis of SLE. [13, 15]

6.2 Hematological Disease

Hematological disease include hematological system involvement, thrombocytopenia and autoimmune hemolytic anemia.

6.3 Skin Disease

A diagnostic skin biopsy should be considered. In SLE, pDC numbers decrease in the blood and accumulate in affected organs, such as lesional skin [11]. The occurrence of the disease may cause disfigurement in the visible light irradiation area, which is emotionally devastating and may increase the psychological burden of the disease.

6.4 Renal Disease

Despite of available anti-inflammatory and immunosuppressive therapies, lupus nephritis is still a major risk factor for morbidity and mortality in systemic lupus erythematosus. Most patients with LN still ends with CKD or ESRD. Even though some patients with systemic lupus erythematosus don't have any symptoms in kidney disease, it is still necessary for them to evaluate kidney function at initial diagnosis and check kidney disease annually [12].

6.5 Musculoskeletal Involvement

True synovitis and arthralgia are common in SLE. Symmetrical polyarthritis involving metacarpophalangeal joint, proximal interphalangeal joint and knee joint. Monoarthritis should prompt assessment of other causes. Erosion is rare and associated with anti cyclic citrullinated peptide antibodies. Periarticular involvement (including tendons and joint capsules) is more common than previously understood and can lead to reducible deformities [17].

7 Conclusion

For the pathological mechanism has not been fully elucidated, methods nowadays are hard to grasp the main contradiction to solve the SLE completely. Therefore, there is an urgent need to elucidate more comprehensive mechanisms, to find new target, to figure out a more advanced detection means, to develop a more accurate grading method and new technologies to eliminate the illness from body and more ways to deal with drug side effects are conducive to disease treatment.

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