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# Hematopoietic Stem Cell Transplantation for Lupus Nephritis

Lupus Nephritis is a kidney infection or an aggravation which is caused due to Systemic lupus erythematosus (SLE) or commonly called Lupus in kidney. SLE is an autoimmune disease which suppresses the immune system/ immune responses, due to its high prevalence it is widely explored by many researchers and scientists and many possibilities are being tried to cure it. Apart from medications and surgeries, cell based therapies are of greater interest in treating Lupus because of their potential for long term suppression of disease. Technique which is promising to be successful in clinics such as 'Hematopoietic stem cell transplantation (HSCT)', where targeting the autoreactive lymphocytes, cells which are resistant to other conventional therapies, and to replace the dysfunctional immune cells with the newly arise immune cells from Hematopoietic stem cell (HSC) are used along with immunosuppressing therapies to treat Lupus. My opinion paper enlightens the advancement in Stem cell therapy combination with immunosuppression treatment and I believe it's a good approach to follow as it provides an effective treatment for lupus.

## Introduction

Systemic lupus erythematosus (SLE) is a complex and heterogeneous autoimmune disease that attacks different healthy body parts and organs like Skin, Joints, Lungs, Heart, Central nervous system and Kidney. When it affects kidney it is known as Lupus Nephritis (LN). SLE is characterized by production of self-reactive antibodies and immune complexes (IC) which deposit in tissues like skin (cutaneous lupus), kidney (lupus nephritis) joints and muscles (rheumatoid lupus), and type 4 III hypersensitivity reaction cause systemic/chronic inflammation that leads to tissue/organ damage. There are a numerous case reports of patients suffering from lupus or other autoimmune diseases receiving an allogeneic or autologous bone marrow transplants for treatment of malignancies. Therapeutic benefit of the procedure was indicated by putting the disease into remission noted by reports. The treatment of lupus nephritis (LN) is same as that of Systemic lupus erythematosus (SLE) because SLE is the cause of lupus nephritis. Hematopoietic stem cell (HSC) are used along with immunosuppressing therapies to treat Lupus. There so many other treatments used for curing lupus like Mesenchymal stem cells (MSCs), Cyclophosphamide (CY) drug and Immunosuppressive treatment used with HSCT.

HSCT aims to deplete self-reactive lymphocytes, immune cells resistant to conventional therapy, and to replace the malfunctioned immune system with a healthy new immune cells arise from hematopoietic stem cells. The primary step in HSCT is mobilization of peripheral

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blood stem cells collected from the bone marrow after treatment with a drug CyC in combination with G-CS. Leukapheresis and cryopreserved are used to collect those cells which express surface antigen CD34. Negative depletion of T-cells, or positive selection of CD34+ cells are used to manipulate the graft in order to eliminate autoreactive clones. Then followed by mobilization and harvesting step, in which the patient undergoes a conditioning protocol, in which high-dose of cytotoxic agents are given. Re-infusion of graft into the patient. Hematopoietic recovery occurs which is then followed by restoring of hematopoiesis after about 10 days of aplasia. The auto-reactive T-cell clones are eliminated in HSCT. Broad spectrum of antibacterial and antifungal prophylaxis were used. Time to neutrophil engraftment was a mean of nine days. By the HSCT the defective 5 cells are replaced by the newly formed immune cells from HSC which helps the body to perform normally.

## Search strategy

The literature survey for my opinion paper was carried out using different databases, catalogues and records such as PubMed, PubMed Central (PMC) present at National Centre for Biotechnology Information (NCBI), Google Scholar, journals and articles present at Leddy library at University of Windsor, Wikipedia and Lupus Foundation of America. Various research papers, articles, review etc. were read to retrieve and understand the complete information about introduction and current advances going on lupus and lupus nephritis along with recent stem cell therapies, immune suppression and therapeutic procedures. Different techniques for treating lupus were studied utilizing above web servers with different keywords and their results obtained from different experiments based on Hematopoietic stem cell transplantation (HSCT) were assessed. Finally, out of thousands of studies mentioned few recent were shortlisted having unexplored data or ongoing mechanism in curing lupus along with future directions in the field of Hematopoietic stem cell transplantation (HSCT).

## Discussion

It is known in lupus after DNA damage cell undergo apoptosis and form an apoptotic body. The exposes/debris of nucleus considered to be as nuclear antigen by the immune cells of the body and start producing self-reactive antibodies against immune cells then the antigen-antibody complex move via blood to different parts or organs of body like skin, joints, kidney brain where it get deposited and an immune complex can initiate an inflammatory reaction known as Type III 6 Hypersensitivity reaction which further leads to damage of organs like kidney. Once, the organ like kidney nephrons are damaged proteins, albumin, lipids, blood easily passed into the urine and cause proteinuria, hypoalbuminemia, lipiduria. hematuria respectively. The defective cells are replaced by the newly formed cells from Hematopoietic stem cell as well as by immunosuppressing. It is important to examine the benefits of Hematopoietic stem cell

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transplantation (HSCT) in clinical or pre-clinical trials before implementing them on the patients. In general, HSCT has become a promising treatment for severe SLE, and SADs. It may be a salvage therapy as well as a disease-controlling procedure. Its effects are both immediate and progressive in nature. HSCT shows efficacy for SLE due to following reasons:

1. the utility of high dose immune suppressants for removal of self-reactive immune system during the process of mobilization and pretreatment;
2. the redistribution of altered cellular and humoral immune network or thymic re-education, development, and regeneration of a new and self-tolerant immune system from HSC;
3. susceptibility gene for SLE trend to negative expression.

In severe SLE with potential use, HSCT combined with immune suppressants, chemotherapeutic drugs, and monoclonal antibody is a newer therapy. Patient should also aware of the risks associated with the treatments like due to pancytopenia or during mobilization and transplantation, high risk of mortality seen immediately after post-HSCT, causes infection and bleeding in the patient. Due to consumption of very high-dose of immunosuppressant- viral or bacterial infections occurred and due to impaired function of regulatory T cells, uncontrolled autoimmune response causes secondary autoimmunity, lymphoma and malignancy. Only patients that have failed all conventional therapy are candidates due to high risk of procedure. There are so many other alternative approaches for curing lupus like MSC transplantation, Cyclophosphamide (CY) drug for mobilization combined with granulocyte colony stimulating factors (G-CSF) and Immunosuppressive treatment (combination of chemo and radiotherapy) used in HSCT. Therefore, I believe that this HSCT therapy holds a lot of potential in treating the lupus patients.

## Future directions

It is clear that HSC transplantation has the potential for substantial therapeutic effects on patients with SLE. Further examination of HSCs must be done to discern the potency of HSCs from these different sources. The source and donor of HSCs will likely prove to be of importance as future studies regarding HSC transplantation are performed. HSCs require a particular microenvironment for maximal suppressive function and for its activation HSC requires additional clarification since the environment which is required for the activation of HSCs is also the pro-inflammatory environment that leads to the pathogenesis of autoimmune diseases. HSCT remains a viable option for patients with severe disease refractory to standard therapy. For proper use of this therapy, careful patient selection and performance is required in experienced centers. It is considered to be a robust bridge for more and better biological therapies in the future, similarly to discovery of the tyrosine-kinase inhibitors that have cancelled most allogeneic transplants for chronic myelogenous leukemia (CML).

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HSCT results in lower mortality rates than allogeneic transplantation mainly due to the absence of graft versus host disease. In severe SLE, HSCT combined with immunosuppressant, chemotherapeutic drugs, and monoclonal antibody has potential use. In my opinion this treatment will be successful in clinical setting because of its efficacy, susceptibility and low mortality. Moreover, most of the 8 studies done on lupus shows HSCT is the viable and effective method of curing lupus as compare to other conventional treatments.

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