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Stem Cell Transplantation in Scleroderma Therapy

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Abstract

The new studies on Scleroderma therebyare Support for using hematopoietic stem cell therapy (HSCT) for SSc , which shows that stem cell transplants can provide better long-term benefits than the standard treatment for patients with severe scleroderma.

Introduction

stem cell transplant A procedure in which a patient receives healthy blood-forming cells (stem cells) to replace their own that have been destroyed by disease or by the radiation or high doses of anticancer drugs that are given as part of the procedure. The healthy stem cells may come from the blood or bone marrow of the patient, from a donor, or from the umbilical cord blood of a newborn baby. A stem cell transplant may be autologous (using a patient's own stem cells that were collected and saved before treatment), allogeneic (using stem cells donated by someone who is not an identical twin), or syngeneic (using stem cells donated by an identical twin).(1)

One of the diseases that now treated by **stem cell transplant** is **scleroderma**

Systemic scleroderma is an autoimmune disorder that affects the skin and internal organs. Autoimmune disorders occur when the immune system malfunctions and attacks the body's own tissues and organs. The word "scleroderma" means hard skin in Greek, and the condition is characterized by the buildup of scar tissue (fibrosis) in the skin and other organs. The condition is also called systemic sclerosis because the fibrosis can affect organs other than the skin. Fibrosis is due to the excess production of a tough protein called collagen, which normally strengthens and supports connective tissues throughout the body.

• The idea behind this kind of investigational therapy is to remove as much of the autoimmune cells as possible and then replace immune function with a subsequent transplant of the patient's own HSC's that were harvested earlier.

The hope is that this HSC transplant (HSCT) yields mature immune cells that are not auto-reactive.(2)

Discussion

1st Study

Methods: Only patients with SSc, treated by HSCT in European phase I–II studies from 1996 up to 2002, with more than 6 months of follow up were included. Transplant regimens were according to the international consensus statements. Repeated evaluations analysed complete, partial, or non-response and the probability of disease progression and survival after HSCT (Kaplan-Meier).

Results: Given as median (range). Among 57 patients aged 40 (9.1–68.7) years the skin scores improved at 6 (n=37 patients), 12 (n=30), 24 (n=19), and 36 (n=10) months after HSCT ($p<0.005$). After 22.9 (4.5–81.1) months, partial (n=32) or complete response (n=14) was seen in 92% and non-response in 8% (n=4) of 50 observed cases. 35% of the patients with initial partial (n=13/32) or complete response (n=3/14) relapsed within 10 (2.2–48.7) months after HSCT. The TRM was 8.7% (n=5/57). Deaths related to progression accounted for 14% (n=8/57) of the 23% (n=13/57) total mortality rate. At 5 years, progression probability was 48% (95% CI 28 to 68) and the projected survival was 72% (95% CI 59 to 75).(3)

2nd Study

Methods: Results for 41 patients included in continuing multicentre open phase I/II studies using HSCT in the treatment of poor prognosis SSc are reported. Thirty seven patients had a predominantly diffuse skin form of the disease and four the limited form, with some clinical overlap. Median age was 41 years with a 5:1 female to male ratio. The skin score was >50% of maximum in 20/33 (61%) patients, with some lung disease attributable to SSc in 28/37 (76%), the forced vital capacity being <70% of the predicted value in 18/36 (50%). Pulmonary hypertension was described in 7/37 (19%) patients and renal disease in 5/37 (14%). The Scl-70 antibody was positive in 18/32 (56%) and the anticentromere antibody in 10% of evaluable patients. Peripheral blood stem cell mobilisation was performed with cyclophosphamide or granulocyte colony stimulating factor, alone or in combination. Thirty eight patients had ex vivo CD34 stem cell selection, with additional T cell depletion in seven. Seven conditioning regimens were used, but six of these used haemoimmunoablative

doses of cyclophosphamide +/- anti-thymocyte globulin +/- total body irradiation. The median duration of follow up was 12 months (3–55).

Result: An improvement in skin score of >25% after transplantation occurred in 20/29 (69%) evaluable patients, and deterioration in 2/29 (7%). Lung function did not change significantly after transplantation. One of five renal cases deteriorated but with no new occurrences of renal disease after HSCT, and the pulmonary hypertension did not progress in the evaluable cases. Disease progression was seen in 7/37 (19%) patients after HSCT with a median period of 67 (range 49–255) days. Eleven (27%) patients had died at census and seven (17%) deaths were considered to be related to the procedure (direct organ toxicity in four, haemorrhage in two, and infection/neutropenic fever in one). The cumulative probability of survival at one year was 73% (95% CI 58 to 88) by Kaplan-Meier analysis.(4)

3rd Study

Method: linical trial conducted in 10 countries at 29 centers with access to a European Group for Blood and Marrow Transplantation–registered transplant facility. From March 2001 to October 2009, 156 patients with early diffuse cutaneous systemic sclerosis were recruited and followed up until October 31, 2013.

Results A total of 156 patients were randomly assigned to receive HSCT (n = 79) or cyclophosphamide (n = 77). During a median follow-up of 5.8 years, 53 events occurred: 22 in the HSCT group (19 deaths and 3 irreversible organ failures) and 31 in the control group (23 deaths and 8 irreversible organ failures). During the first year, there were more events in the HSCT group (13 events [16.5%], including 8 treatment-related deaths) than in the control group (8 events [10.4%], with no treatment-related deaths). At 2 years, 14 events (17.7%) had occurred cumulatively in the HSCT group vs 14 events (18.2%) in the control group; at 4 years, 15 events (19%) had occurred cumulatively in the HSCT group vs 20 events (26%) in the control group. Time-varying hazard ratios (modeled with treatment × time interaction) for event-free survival were 0.35 (95% CI, 0.16-0.74) at 2 years and 0.34 (95% CI, 0.16-0.74) at 4 years. (5)

Conclusion

The previous Studied Show That HSCT found to significantly improve survival and quality of life, compared to the other therapies that used in scleroderma.

References

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