Efficacy and Safety Comparison of Calcineurin Inhibitors Used for GVHD Prophylaxis in Hematopoietic Stem Cell Transplantation in Children with Thalassemia

**Topic:** 22. Stem cell transplantation - Clinical

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**Background:**
For the prophylaxis of graft versus host disease (GVHD), the calcineurin inhibitors are the backbone of the therapy and cyclosporine is preferred more frequently than tacrolimus in pediatric hematopoietic stem cell transplantation. However, although the use of tacrolimus has increased recently, the number of studies comparing these two drugs in the pediatric patient group is limited.

**Aims:**
In this study, the efficacy and safety of the cyclosporine and tacrolimus were compared in pediatric patients transplanted for thalassemia.

**Methods:**
In this study, 129 pediatric patients who underwent hematopoietic stem cell transplantation with the diagnosis of thalassemia in our center between January 2017 and December 2020 were divided into two groups according to the type of calcineurin inhibitor used in GVHD prophylaxis. In the prophylaxis of GVHD, the patients in the first group used cyclosporine (n=68), the patients in the second group used tacrolimus (n=61), and the effects of the groups on the transplantation process were compared retrospectively. In all patients, methotrexate and anti-thymocyte globulin (ATG) were used in addition to cyclosporine or tacrolimus for GVHD prophylaxis. A myeloablative regimen was used in all transplants. Patients who were followed up for at least 7 months after transplantation were evaluated in terms of transplantation related complications and possible calcineurin inhibitor related side effects.

**Results:**
Median age of patients was 81 months (10-263 months), female/male ratio was 1.1 (69/60), donor types MUD 72 patients (56%), MSD 30 patients (39%), and MPD 7 patients (5%) was detected. Bone marrow in 65 (50%) patients, peripheral stem cells in 53 (41%) and bone marrow-cord blood combinations in 11 (9%) patients were used as stem cell source. There was no statistically significant difference between the two groups in terms of age, gender, donor type and stem cell source. The median follow-up period of all patients was 31 months (7-54 months).

Despite the use of GVHD prophylaxis, it was determined that at least grade 2 acute GVHD developed in 29 patients. Of these patients, 12 had only gut, 10 had only skin, 6 had combined gut and skin, and one had only liver GVHD. There was no significant difference between the groups in terms of acute GVHD development, GVHD stage and involvement sites. During the acute GVHD follow up period, only 3 of all patients developed chronic GVHD, and all of these patients were in the cyclosporine group. There was no significant difference between the groups in terms of engraftment syndrome, veno-occlusive disease, CMV reactivation, PRES and graft rejection.
Neurotoxicity in 12 (cyclosporine n=7, tacrolimus n=5) and nephrotoxicity in 18 (cyclosporine n=4, tacrolimus n=14) patients were observed as possible side effects associated with the use of calcineurin inhibitors. While there was no difference between the two groups in terms of neurotoxicity, more nephrotoxicity developed in patients using tacrolimus (p=0.013).

Summary/Conclusion:

There was no difference in efficacy between the use of cyclosporine or tacrolimus for GVHD prophylaxis in pediatric stem cell transplantation for thalassemia. In terms of side effects, more nephrotoxicity was observed in patients receiving tacrolimus. In the selection of calcineurin inhibitor, this difference should be taken into account according to the clinical condition of the patient.