Tandem High-dose Chemotherapy with Busulfan-melphalan and Thiotepa-cyclophosphamide and Autologous Stem Cell Transplantation in Combination with 131I-MIBG Therapy for High-risk Neuroblastoma

Young Kwon Koh1, Aae Jin Kang1, Sung Han Kang1, Hyery Kim1, Ho Joon Im1 and Kyung-Nam Koh1

1Division of Pediatric Hematology/Oncology, Department of Pediatrics, Asan Medical Center Children’s Hospital, University of Ulsan College of Medicine, Korea

Background: 131I-MIBG has been used as a solitary or in combination with chemotherapy for the treatment of high-risk neuroblastoma. This study aimed to evaluate the feasibility and effectiveness of tandem high-dose chemotherapy and autologous stem cell transplantation (HDCT/ASCT) with busulfan-melphalan and thiotepa-cyclophosphamide combined with targeted radiotherapy using 131I-MIBG for high-risk neuroblastoma.

Materials and Method: 20 patients were diagnosed with high-risk neuroblastoma in our institution between October 2013 and April 2019. Patients were intended to receive 8 to 10 cycles of induction chemotherapy and tandem HDCT/ASCT combined with 131I-MIBG therapy prior to the second HDCT/ASCT. For the first HDCT/ASCT regimen, patients received busulfan/melphalan. The second HDCT regimen included thiotepa/cyclophosphamide.

Results: 20 patients received the first HDCT and 131I-MIBG treatment. 17 patients completed the second HDCT/ASCT. 3 patients did not receive the second HDCT due to 2 patients developed pulmonary hypertension and one patient refused. The median dose of 131I-MIBG was 10.9mCi/kg. After the second HDCT/ASCT, 19 patients received local radiotherapy at a median dose of 2100cGy. 16 patients received post-HDCT maintenance therapy with 13-CRA, IL-2, dinutuximab. The 5 years OS and EFS rates were 73% and 62% retrospectively. Six patients (30%) experienced disease relapse, and three patients (15%) died of disease progression and two patients (10%) died of treatment-related mortality (TRM). One patient died of sepsis after lung transplantation for lung graft-versus-host disease and one patient died of fungal pneumonia after the second HDCT/ASCT. One patient died of treatment-related MDS. Among 17 evaluable patients, 5 patients (29%) developed hypothyroidism, 2 patients (12%) had CKD, 3 patients (18%) had growth failure, and 3 patients (18%) had pulmonary hypertension.

Conclusion: Tandem HDCT/ASCT using busulfan-melphalan and thiotepa-cyclophosphamide combined with 131I-MIBG therapy was feasible and effective for high-risk neuroblastoma patients. But more efforts are needed to reducing TRM.

Keywords: Neuroblastoma, 131I-MIBG, Autologous stem cell transplantation, High-dose chemotherapy