HA-01

The influence of conditioning regimen on recovery of fertility following allogeneic stem cell transplantation in aplastic anemia patients

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Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is currently considered the golden standard treatment for young patients with aplastic anemia. Recovery of fertility (FR) after allo-HSCT has a significant influence upon the quality of life in the transplant survivors. The aim of the study was to evaluate the impact of conditioning regimen on fertility recovery in AA patients.

Patients and methods

A total of 62 patients with AA who survived for, at least, 1 year following allo-HSCT was included in our study. Most patients received busulfan-based (Bu) conditioning regimen, i.e., 39 patients (64%, group 2), and other 22 patients (36%) received cyclophosphamide-based (Cy) regimen (group 1). The median follow-up period was 5.5 (0.82-20) years. Most patients in group 1 were males (n=13, 57%). Nineteen (82%) patients received allo-HSCT from matched related donor (MRD); 4 (17%), from matched unrelated donor (MUD). The median age at allo-HSCT was 25 (17-38) years. Severe chronic graft-versus-host disease (GVHD) was registered in 2 cases (10%). Most patients in group 2 were females (n=21, 55%). Twenty-one patient (54 %) received allo-HSCT from MUD, 18 (46%) were transplanted from MRD. Median age at allo-HSCT was 28 (17-50) years. Severe GVHD cases were registered in 3 cases (8%).

Results

Twenty-five patients (41%) had children before allo-HSCT. Twenty-three patients (38 %) did not plan to have children in the near future. 7% of patients underwent hysterectomy before allo-HSCT. Recovery of the menstrual cycle after allo-HSCT has been reported in 46% of cases (14 patients). Median time period from allo-HSCT to the menstrual cycle recovery was 2.3 (0.24-4.48) months. In 17 patients (54%), the cycle was not restored. Among the females who underwent allo-HSCT, nine pregnancies were registered which resulted in healthy live births. In the Bu-based group, one spontaneous pregnancy was registered, and one patient underwent IVF with a donor egg (3%). The men from the first group (Cy-based conditioning) had 5 children after allo-HSCT, and 6 children were born of them in second group (Bu-based conditioning). One patient from group 2 had to use IVF twice. A total of 21 pregnancies were registered. When analysing possible risk factors, only busulfan-based conditioning was a significant risk factor for impaired FR ($p<0.03$) and menstrual cycle recovery ($p<0.03$). Neither age of patient, type of donor, nor chronic GVHD had significant impact on fertility.

Conclusion

In our study, usage of busulfan in the conditioning regimen had a statistically significant impact upon recovery of fertility and the menstrual cycle after allo-HSCT.

Keywords

Aplastic anemia, hematopoietic stem cell transplantation, conditioning regimen, fertility.

Влияние режима кондиционирования на фертильность пациентов с апластической анемией после аллогенной трансплантации костного мозга

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Введение

Аллогенная трансплантация гемопоэтических стволовых клеток крови (алло-ТГСК) является «золотым стандартом» лечения апластической анемии (АА) у пациентов молодого возраста. Сохранение фертильности после алло-ТГСК во многом определяет качество жизни пациентов. Цель исследования – оценить влияние препаратов режима кондиционирования на фертильность пациентов с апластической анемией после аллогенной трансплантации костного мозга.

Пациенты и методы

В исследование включены 62 пациента с АА, прожившие более 1 года после алло-ТГСК: большинство пациентов получали бусульфан-содержащий режим кондиционирования 39 пациентов (63%) (группа 2), остальные 23 пациента (37%) получили режим кондиционирования на основе циклофосфана (группа 1). Медиана наблюдения составила 5,5 (0,82-20) лет. В группе 1 преобладали мужчины 13 (57%), 19 (82%) пациентов получили алло-ТГСК от полностью совместимого родственного донора, 4 (17%) – от полностью совместимого неродственного донора. Медиана возраста на момент алло-ТГСК составила 25 (17-38) лет. Тяжелая хроническая реакция «трансплантат против хозяина» (хрРТПХ) регистрировалась у 2 пациентов (10%). В группе 2 преобладали женщины 21 (55 %), 21 пациент (54%) получил алло-ТГСК от полностью совместимого неродственного