PULMONARY PERFORMANCE IN PATIENTS OF HEMATOPOIETIC STEM CELL TRANSPLANTATION

Mohammed Yunis[1], Engy Osman[2], Ahmad Darwish[1], Khaled Fathy[3], Mona Mohammed Hafez[4]

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ABSTRACT

Background: In adolescents and young adults who have refractory cancers, bone marrow failure syndromes, or primary immunological deficiencies, hematopoietic stem cell transplantation (HSCT) is a potentially curative therapy option. **(Rotz et al., 2017)**. It has been observed that during the first year following hematopoietic stem cell transplantation (HSCT), up to 85 percent of pediatric patients experience a decline in their pulmonary function (PF).

Aim: The purpose of this research is to assess lung function by spirometry to detect any changes which may affect prognosis and quality of life after transplantation.

Methods: Children 5-18 years old undergoing bone marrow transplantation at Mansoura University Children's Hospital were enrolled during the years 2022 and 2023. Pulmonary function tests by spirometry were done for each patient pre and post HSCT.

Results: A total of 25 children, all of whom had BMT performed at either MUCH or OCMU and who had a median age of 8 years, of which 60% were males and 40% were females, were subjected to an evaluation. Our study revealed that there was a significant difference before and after transplant regarding FVC, where patients had lower FVC after transplant compared to that before transplant.

Regarding FEV1, there was a significant difference before and after transplant, where patients had lower FEV1 after transplant compared to that before transplant. There was no significant difference as regard FEV1/FVC before and after transplant.

Conclusion: Outcomes drawn from the present investigation are that spirometry is a good tool to diagnose pulmonary affection in patients of HSCT who received certain chemotherapeutics during transplant.

Keywords: Bone marrow transplantation, pulmonary function tests, conditioning, cyclophosphamide, Busulfan.

1 Pediatric Hematology/Oncology & Bone Marrow Transplantation Unit, Pediatric Department, Faculty of Medicine, Mansoura University, Egypt.
2 Pediatric Pulmonology & Immunology Unit, Pediatric Department, Faculty of Medicine, Mansoura University, Egypt.
3 Pediatric Neurology Unit, Pediatric Department, Faculty of Medicine, Mansoura University, Egypt.
4 Pediatric Cardiology Unit, Pediatric Department, Faculty of Medicine, Mansoura University, Egypt.
Email: myunis43@gmail.com

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INTRODUCTION

Many childhood and early adult cancers, bone marrow failure syndromes, and primary immunological deficiencies have a good chance of being cured by hematopoietic stem cell transplantation (HSCT) **(Rotz et al., 2017)**.

A staggering eighty-five percent of pediatric patients have experienced decreased pulmonary function (PF) in the first year following hematopoietic stem cell transplantation (HSCT). The patients who underwent HSCT were the subject of a retrospective, population-based investigation at a single institution. The effects of time and transplantation-related factors on PF were studied. Thirty patients were enrolled in the long-term study, which had a median (range) observation period of 3.3 (.2 to 16.8) years. Within the first three to six months after HSCT, 62% of patients saw a 10% or more loss in lung function. Acute graft-versus-host disease (GvHD) was highly linked with the decrease in forced expiratory volume in 1 second and forced expiratory volume in 1 second/forced vital capacity. Chronic GvHD was also linked to a lower risk of PF, as was a malignant diagnosis, busulfan-based conditioning, older age for both the patient and donor, a female donor to male recipient ratio, and a younger age for the recipient. (GvHD) seems to be linked to mild to moderate loss in (PF). This suggests that the etiology of the decline in PF in children after HSCT involves alloreactivity to a significant degree. ***(Hilde Hylland Uhlving , et al, 2013).***

MATERIALS AND METHODS

Aim of work

This research aims to evaluate lung function by spirometry to detect any changes which may affect prognosis and quality of life after transplantation.

Study design and participants

- History: Thorough history was taken for all patients (including age, sex, cause of transplantation) and risk factors for pulmonary disease as asthma, anemia.
- Examination (including growth parameters, general examination)
- Pulmonary Functions Testing (Spirometry) (Medisoft) at pediatric allergy and clinical immunology unit in MUCH:

- Forced vital capacity [FVC].
- Forced expiratory volume in 1 second [FEV1].
- FEV1/FVC ratio.

The interpretation is based on the professional opinion of a specialist and includes the identification of a pattern (obstructive, restricted, mixed, and normal) as well as the grading of the severity of the pattern in accordance with international norms ***(Culver et al., 2017)***. Combining patient history, symptoms, and PFT values led to a definitive diagnosis ***(Galie et al., 2016; Martinez et al., 2017)***.

Exclusion criteria:

- Patients with chronic lung disease
- Pre transplant patients proven to have lung disease before HSCT.

Ethical considerations

- The protocol has received approval from the Ethical Committee of Faculty of Medicine, Mansoura University at 30/11/2021 with code number MD.21.11.558.R1.
- All participating caregivers provided verbal and written informed permission.

Statistical analysis

For this study, we used Windows and SPSS for Social Science (Standard version 21) to analyze the data. First, a one-sample Kolmogorov-Smirnov test was performed to ensure that the data were normally distributed. Numerical and percentage descriptions were used to describe qualitative data. Chi-square tests were used to look for patterns of association between categorical variables. For properly distributed data, the continuous variables were shown as mean ± SD (standard deviation), and for non-normally distributed data, the median (min-max) was used. Student t test was used to compare the two groups.

Continuous data were correlated with the help of Pearson correlation.

The level of significance for all of the aforementioned statistical tests is set at 5%. When p was ≤ 0.05, the findings were considered to be significant. The more significant the findings, the lower the p-value.

RESULTS

Twenty-five patients at the Mansoura University Children's Hospital and the Mansoura University Oncology Center participated in this study with 60% of patients were men and 40% were women, having an average age of 8 years and a weight of 26 kg on average. Table (1).

As regard disease related data in studied patients in this study, only 1 case received transplant for a non-malignant disorder (Beta thalassemia), 4 cases had AML, 9 cases had Hodgkin lymphoma and 11 cases had neuroblastoma with a median duration from diagnosis to transplantation was 24 months. Eighty percent of patients underwent autologous bone marrow transplant, while 20 percent underwent allogenic bone marrow transplant. Table (2)

As regards GVHD related data during transplant, 20% of cases received GVHD prophylaxis (allogenic transplant) and 80% of cases didn't. Only one patient developed acute GVHD while chronic GVHD wasn't reported in any case. Positive asthma history was detected in only 2 cases. Table (3).

Regarding the chemotherapeutic agents used either before or during marrow transplant that have potential cardiac and pulmonary toxicity including cyclophosphamide, busulfan, melphalan, carmustine and doxorubicin shown in Table (4).

As regards results of pulmonary function tests before and after transplant, there was a significant difference before and after transplant regarding FVC%, where patients had lower FVC% (82.28 ± 12.47) after transplant compared to that before transplant (84.92 ± 12.62) .

Regarding FEV1, there was a significant difference before and after transplant, where patients had lower FEV1% (75.96 ± 17.66) after transplant compared to that before transplant (79.60 ± 18.11).

There was no significant difference as regard FEV1/FVC before and after transplant.

A reduced FEV1/FVC% and a FEV1>80% are the diagnostic criteria for obstructive impairment.

A restrictive impairment is characterized as having a normal or enhanced FEV1/FVC% while having an FVC that is less than 80%.

In patients who had a reduced forced vital capacity (FVC), a reduced (FEV1), and a normal FEV1/FVC%, restrictive impairment paired with obstructive involvement was taken into consideration. Table (5).

Table (1): The demographic data pertaining to the group under investigation:

Variables	Study cases N = 25	
Gender	**N**	**%**
Males	**15**	**60**
Females	**10**	**40**
Age (years)		
Mean ± SD	**9.8 ± 4.23**	
Median (Range)	**8 (5 - 17)**	
Weight (Kg)		
Mean ± SD	**34.16 ± 17.6**	
Median (Range)	**26 (17 – 70)**	

Table (2): Disease related data in the cases of the study

Variables	Study cases N = 25	
Primary disease	**N**	**%**
AML	**4**	**16**
Hodgkin	**9**	**36**
Neuroblastoma	**11**	**44**
thalassemia	**1**	**4**
Time from diagnosis to BMT (months)		
Mean ± SD	**24.76 ± 9.82**	
Median (Range)	**24 (12 - 48)**	
Conditioning regimen	**N**	**%**
BEAM	**9**	**36**
Bu-Alk	**11**	**44**
Bu-Cy	**5**	**20**
Type transplant	**N**	**%**
Auto	**20**	**80**
Allo	**5**	**20**

Table (3): Graft versus host disease data during transplant:

Variables	Study cases N = 25	
GVHD prophylaxis	**N**	**%**
No	**20**	**80**
Yes	**5**	**20**
Acute GVHD	**N**	**%**
No	**24**	**96**
Yes	**1**	**4**
Chronic GVHD	**N**	**%**
No	**25**	**100**
Yes	**0**	**0**
Asthma history	**N**	**%**
No	**23**	**92**
Yes	**2**	**8**

Table (4): Chemotherapeutics used during and before BMT:

Variables	Study cases N = 25	
	N	%
Cyclophosphamide	**5**	**20**
Busulfan	**16**	**64**
Melphalan	**20**	**80**
Carmustine	**9**	**36**
Cyclophosphamide before transplant	**18**	**72**
Doxorubicin before transplant	**15**	**60**

Table (5): Pulmonary function tests before and after transplant:

Variables	Before transplant (N=25)	After transplant (N=25)	P Value
FVC% (mean±SD)	**84.92 ± 12.62**	**82.28 ± 12.47**	**0.016***
FEV1% (mean±SD)	**79.60 ± 18.11**	**75.96 ± 17.66**	**0.026***
FEV1/FVC (mean±SD)	**92.68 ± 15.37**	**91.60 ± 16.36**	**0.562**

DISCUSSION

A considerable decline in pulmonary function (PF) has been shown in as many as 85% of pediatric individuals within the initial year following hematopoietic stem cell transplantation (HSCT) ***(Hilde Hylland Uhlving, et al, 2013)***.

We conducted a prospective observational study over 18 months to evaluate the lung function by spirometry to detect any changes which may affect prognosis and quality of life after bone marrow transplantation.

Participating in this study were a total of 25 individuals who were at Mansoura University Children's Hospital and oncology center Mansoura university for bone marrow transplantation either autologous or allogenic.

Our study revealed that there was a significant difference before and after transplant regarding FVC, where patients had lower FVC after transplant compared to that before transplant.

Regarding FEV1, there was a significant difference before and after transplant, where patients had lower FEV1 after transplant compared to that before transplant. There was no significant difference as regard FEV1/FVC before and after transplant.

This was in concordance with Hilde Hylland Uhlving who conducted study on one hundred thirty patients were monitored for a total of 3.3 (ranging from 0.2 to 16.8) years on average (median). During the initial three to six months following HSCT, the patients' lung function decreased by more than ten percent in sixty-two percent of the cases. There was a significant correlation between acute graft-versus-host disease (GvHD) and a decrease in forced expiratory volume in one second as well as forced expiratory volume in one second/forced vital capacity ***(Hilde Hylland Uhlving, et al, 2013)***.

This research has a few caveats. Since this was a study conducted at one center with a small sample size, more extensive, larger-scale investigations are needed to confirm the results of this one.

CONCLUSION

Following a bone marrow transplantation, there is a possibility that pulmonary function tests will be impacted due to the chemotherapeutics that are used in the transplantation process. These chemotherapeutics have the potential to produce pulmonary toxicity. This conclusion may be drawn from the findings of the current study.

LIST OF ABBREVIATIONS

AML: Acute myeloid leukemia
FEV1: Forced expiratory volume 1
FVC: Forced vital capacity
HSCT: Hematopoietic stem cell transplantation.
MUCH: Mansoura University Children's Hospital
OCMU: Oncology center Mansoura University.
PFTs: Pulmonary function tests

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