

Protective environment in hematopoietic cell transplantation centers: results of a survey of the Polish Federation of Bone Marrow Transplant Centers

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Introduction

Hematopoietic cell transplantation (HCT) is one of the most immunosuppressive treatments performed currently in medicine. High level of protective environment is required for patients undergoing HCT to ensure safety of this treatment in the transplant setting. International guidelines on transplant protective environment for health-care facilities regarding hospital room design and ventilation were proposed as a set of 10 Global Recommendations on Protective Environment (GRPE) in 2009 [1, 2]. These guidelines were coordinated by the Center for International Blood and Marrow Transplant Research (CIBMTR), with the participation of the National Marrow Donor Program (NMDP), the American Society for Blood and Marrow Transplantation (ASBMT), the European Society for Blood and Marrow Transplantation (EBMT), the Infectious Diseases Society of America (IDSA), the Canadian Blood and Marrow Transplant Group (CBMTG), the Centers for Disease Control (CDC), the Association of Medical Microbiology and Infectious Disease (AMMI), and the Society for Healthcare Epidemiology of America (SHEA).

The objective of this study was to determine the current status on protective environment for HCT recipients in Polish transplant centers and to report current practices in the hospital transplant setting, with focus on room design and ventilation, as well as their agreement with GRPE recommendations.

Methods

Study design

During the Transplant Workshop of the Polish Federation of Bone Marrow Transplant Centers in Poznań, on October 12, 2019, a survey on antimicrobial prophylaxis and protective transplant environment was carried out, with one questionnaire administered per transplant center. The part of the survey on protective environment was based on the GRPE recommendations [1, 2] and was compared with the results obtained from the survey of EBMT centers, performed in 2012 [3]. Results of the first part of the survey on antimicrobial prophylaxis have been analyzed elsewhere [4].

Definitions

High efficiency particulate air (HEPA) filter – a high-efficiency particulate air filter, with 99.97% efficiency in removing particles $\geq 0.3 \mu\text{m}$ in diameter with safe ventilation of ≥ 12 air exchanges/hour. A laminar air flow room – a room containing HEPA-filtered air that moves in a parallel unidirectional flow, such that the air enters the room from one side and exits this room from the other side. Combined room – a room designed for patients for isolation in order to protect them against airborne infections and provide specific protective environment by means of positive air pressure and laminar air flow [3].

Bioethical issues

No Bioethical Committee consent was necessary for this study, as no study was performed on patients; all participants of the survey are coauthors of this manuscript and give their agreement for publication.

Statistical analysis

Categorical variables were compared with the chi-square test. Odds ratio (OR) and confidence intervals (95% CIs) were calculated for the difference in the rates of positive responses between this survey and the EBMT survey [3]. All reported *p*-values are two-sided; *p* < 0.05 was considered statistically significant.

Results and discussion

Center participation

All 23 Polish HCT centers participated in the survey, including six pediatric and 17 adult centers. The summary of responses provided by the centers, in comparison to the positive responses of the EBMT centers, is shown in Table I.

HEPA filters

Central or point-of-use HEPA filters with 99.97% efficiency for removing particles $\geq 0.3 \mu\text{m}$ in diameter ensuring safe ventilation of ≥ 12 air exchanges/hour is a standard of care in all Polish centers, both for allo-HCT and auto-HCT, including centers that perform auto-HCT only. All but one center have air-conditioning systems (ACs) exclusively designed for the transplant unit, and in the case of the single nonconforming center, the AC is shared with the hospital pharmacy. The majority (78%) of the centers declare regular replacement of HEPA filters, with variable frequency, but at least once a year. This regularity is higher than those reported by the EBMT centers (odds ratio [OR] = 3.8; 95% CI = 1.3–11.0; *p* = 0.018) [3]. Moreover, the majority of centers have a written procedure for filter maintenance and removal. GRPE recommendations require that filters should be replaced regularly based on manufacturers' recommendations, and, when there is ongoing construction, filtration efficiency should be monitored frequently to best determine the appropriate time for replacement [1–3, 5].

Positive air pressure

Consistent positive air pressure differential between the patient's room and the hallway of $\geq 2.5 \text{ Pa}$ is required. Only 34% of centers are equipped with a permanently installed device or mechanism to constantly monitor the differential air pressure between the room and the corridor, and even fewer centers are capable of monitoring the air pressure in the anteroom, in addition to the air pressure in the patient's room. This rate is, however, exactly the same as in the EBMT survey [3]. Additionally, in 56% of centers, the

Table I. Overall positive results of the survey with respect to global recommendations on Protective Environment (GRPE)

GRPE	Grading	Survey question	Positive response		OR, p
			Poland, 2019 (n =23)	EBMT, 2012 (n =177*)	
1. Ventilation: ≥ 12 air changes per hour	AIII	Does the room have at least 12 air changes per hour?	23 (100%)	126 (71.2%)	ND
2. Central or point-of-use HEPA filters with 99.97% efficiency for removing particles $\leq 0.3 \mu\text{m}$ in diameter	AIII	Are your patient rooms equipped with HEPA filters?	23 (100%)	176 (99.4%)	ND
3. Filters should be replaced regularly based on manufacturers' recommendations, and, when there is ongoing construction, filtration efficiency should be monitored frequently to best determine the appropriate time for replacement	AIII	How often are the filters changed? (Response: regularly, at least once per year)	18 (78.3%)	52 (48.6%)	OR =3.8, p =0.018
		Do you have a written procedure for filter maintenance and removal?	15 (65.2%)	95 (53.7%)	OR =1.6, p =0.41
		Is a sensor monitor installed in the patient room, which is used to determine when the HEPA filters require changing?	8 (34.8%)	32 (18.1%)	OR =2.4, p =0.10
4. Directed airflow so that air intake occurs at one side of the room and air exhaust occurs at the opposite side	BIII	Is the airflow directed so that air intake occurs at one side of the room, while the air exhaust occurs at the opposite side?	13 (56.5%)	105 (59.3%)	OR =0.9, p =0.97
5. Consistent positive air pressure differential between the patient's room and the hallway of $\geq 2.5 \text{ Pa}$	BIII	Is there a permanently installed device/mechanism to constantly monitor the differential air pressure between the room and the corridor?	8 (34.8%)	68 (38.4%)	OR =0.9, p =0.91
6. Well-sealed rooms (e.g., filling the gaps between walls and windows, outlets, floor, and ceiling) should always be used for HCT patients to prevent infiltration of air from outside the room, which could allow entry of spores and hinder maintenance of proper pressure differential	BIII	Are the room windows sealed to eliminate infiltration from outside?	19 (82.6%)	125 (70.6%)	OR =2.0, p =0.33
		Do the protective environment rooms have monolithic ceilings?	12 (52.2%)	62 (35.0%)	OR =2.0, p =0.16
		Are all plumbing pipes in the room sealed around wall penetrations?	12 (52.2%)	91 (51.4%)	OR =1.0, p =0.94
7. Continuous pressure monitoring, especially while rooms are occupied	BIII	Is there an air pressure-monitoring device/mechanism in the anteroom, in addition to the air pressure in the patient's room?	5 (21.7%)	31 (17.5%)	OR =1.3, p =0.83
8. Self-closing doors to maintain constant pressure differentials	BIII	Are there self-closing doors to maintain constant pressure differentials?	10 (43.5%)	66 (37.3%)	OR =1.3, p =0.72
9. Monitoring systems that will set off an alarm when the pressure differential between any protective environment room and adjacent hallway or anteroom falls to $< 2.5 \text{ Pa}$, to alert staff to possible engineering failures	CIII	Is there a monitoring system that will set off an alarm when the pressure differential between any protective environment room and adjacent hallway or anteroom falls to $< 2.5 \text{ Pa}$, to alert staff to possible engineering failures?	3 (13.6%)	60 (33.9%)	OR =0.3, p =0.073
10. To enable the nursing staff to observe the HCT recipient even when the doors are closed, windows can be installed in either the door or the wall of the HCT recipient's room	CIII	Is the nursing staff able to observe the patient even when the doors are closed?	17 (73.9%)	109 (61.6%)	OR =1.8, p =0.35

*Not all centers responded to all questions; EBMT – European Society for Blood and Marrow Transplantation; OR – odds ratio; ND – not done; HEPA – high efficiency particulate air; HCT – hematopoietic cell transplantation

airflow is directed such that air intake occurs at one side of the room, while the air exhaust occurs at the opposite side. However, only three (13.6%) centers have a monitoring system that sets off an alarm, especially while rooms are occupied, when the pressure differential between any protective environment room and the adjacent hallway or anteroom falls to <2.5 Pa, in order to alert the staff to possible engineering failures. Nevertheless, these figures are also comparable to the results of the EBMT survey [3].

Well-sealed rooms

Rooms having monolithic ceilings and well-sealed walls and floor should always be used for HCT patients to prevent infiltration of air from outside the room, which could allow entry of spores and hinder maintenance of proper pressure differential. This is also relevant for any plumbing pipes in the room and anteroom. More than half of the centers reported having these technological solutions, with the rate being comparable to the results of the EBMT survey [3].

Self-closing doors

In order to maintain constant pressure differentials, self-closing doors additionally can secure the protective environment. This is a routine in 43.5% Polish centers. In European centers, it is not more frequent [3].

Observing HCT recipients

In a vast majority of centers, the nursing staff is able to observe the HCT recipient even when the doors are closed. This is possible due to the presence of monitoring systems with cameras; in other centers, windows are installed in either the door or the wall of the HCT recipient's room.

Clinical implications of results of the survey

All Polish transplant centers together have created the Polish Federation of Bone Marrow Transplant Centers and actively cooperate at the organizational, medical, educational, and scientific levels. This survey shows that there are some differences in technological solutions among the centers. The differences might result from the different periods of establishment of transplant units: possibly, newer units are built more innovatively and equipped better than the older ones. It should be kept in mind that the survey was answered by physicians exclusively, without contact with supporting technical staff. It is highly probable that physicians and other health-care personnel of the transplant unit do not have access to the necessary information on technical issues in their own center. Nevertheless, all centers ensure proper isolation of the transplant patient, as well as proper room ventilation with the use of HEPA filters. The quality of medical service was additionally confirmed by the first accreditations for chimeric antigen receptor (CAR) T-cell therapy in several Polish transplant centers [6, 7].

The limitation of the study is the small number of transplant centers in Poland, disabling any further comparisons, e.g., pediatric vs adult centers. Furthermore, the survey was not aimed at any microbiological procedures ensuring protective environment. Nevertheless, regular microbiological screening for bacterial and fungal colonization should be performed inside the ward.

Conclusion

The results of this survey confirm that safe and protective patient isolation and protective environment are provided in all Polish transplant centers at the level that meets the required international standards.

Authors' contributions

JS, LG – design of the study and writing the manuscript. JS, LG, AŁ, KC – performing the survey. All authors – critical review and final approval.

Conflicts of interest

All authors have no conflicts of interest to disclose with respect to this paper.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

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