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Review of Antimicrobial Prophylaxis in Patients Undergoing Hematopoietic Stem Cell Transplantation

By

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Essay

A protocol submitted for partial fulfillment of M. Sc. Degree in Clinical Hematology

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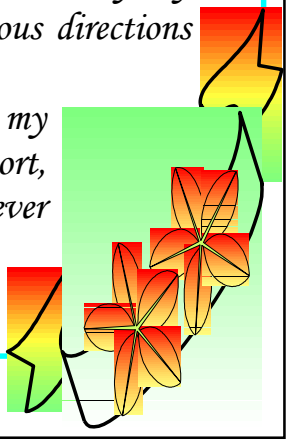
Abd Elsalam Attallah Abd Elrazek



Content

List of Abbreviations

ANC	: Absolute neutrophil count
ATS	: American Thoracic Society
BMT	: Bone Marrow Transplantation
CAMs	: Cell adhesion molecules
CDI	: Clostridium difficile infection
CR	: Complete Remission
CVCs	: Central venous catheters
Cy	: Cyclophosphamide
EBV	: Epstein- Barr virus
ECM	: Extracellular matrix components
G6PD	: Glucose-6-phosphate dehydrogenase
GVHD	: Graft versus host disease
GVHD	: Graft-versus-host disease
GvHD	: Graft- versus- host disease
HCT	: Hematopoietic cell transplantation
HCV	: Hepatitis C virus
HSCT	: Hematopoietic stem cells transplantation
HSV	: Herpes simplex virus
IL	: Interleukin
IPI	: Invasive pneumococcal infection
LAF	: Laminar Air Flow
MHC	: Major histocompatibility complex
MMR	: Measles, mumps and rubella
MRSA	: Methicillin-resistant Staphylococcus aureus
OS	: Overall survival
PBSCs	: Peripheral blood stem cells
PTLD	: Post Transplant Lymphoproliferative Disease

List of Abbreviations (Cont.)

SCID	: Severe combined immunodeficiency
TBI	: Total body irradiation
TCD	: T Cell Depleted
TDT	: Tetanus diphtheria toxoid
UCB	: Umbilical cord blood
URI	: Upper respiratory infection
VOD	: Veno-occlusive disea
VZV	: Varicella-zoster virus

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Introduction:

Hematopoietic stem cells transplantation (HSCT) refers to any procedure where HSCT of any donor type and any source are given to a recipient with the intention of repopulating and replacing the hemopoietic system in total or in part. Stem cells can be derived from bone marrow, peripheral blood or cord blood. Hematopoietic stem cell transplant (HSCT) as a treatment for diseases has been attempted sporadically since the late nineteenth century. Many of the early applications involved feeding or injection of BM into patients with a variety of ailments, such as a several types of anemia, leukemia and chlorosis ***(Quine, 1986).***

Bone Marrow Transplantation (BMT) has been described as both intensive investigational therapy for end-stage disease and as standard curative treatment for some malignant and non-malignant condition. There are three major types of BMT, syngeneic, allogeneic and autolougs, so named to indicate the source of healthy marrow that is obtained and then transplanted into the patient ***(Bakitas, 1991).***

Patients undergoing allogeneic stem cell transplantation are highly susceptible for acquisition

and reactivation of infectious diseases. A variety of bacteria, fungi, viruses and protozoa can induce potentially lethal disease during distinct phases of transplantation. The susceptibility of the host for infections is influenced by the underlying disease including preceding courses of antineoplastic therapy, the intensity and compound of conditioning therapy, and the degree of human leukocyte antigen (HLA)-conformity between stem cell donor and recipient. Furthermore, intensity and duration of Graft- versus-host disease (GvHD) prophylaxis and the manifestation of (GvHD) contribute substantially to susceptibility for severe infections ***(Cornely, Schirmacher, 2001).***

In The past decade, modifications in HSCT management and supportive care have resulted in changes in recommendations for the prevention of infection in HSCT patients. These changes are fueled by new antimicrobial agents, increased knowledge of immune reconstitution, and expanded conditioning regimens and patient populations eligible for HSCT. Despite these advances, infection is reported as the primary cause of death in 8% of autologous HCT

patients and 17% to 20% of allergenic HCT recipients ***(CIBMTR, 2009).***

Susceptibility to infection has posed one of the most formidable challenges in the clinical management of patients undergoing hematopoietic cell transplantation (HCT) from the earliest days of this treatment.

A variety of advances in infection control have permitted major strides in the supportive care of transplant recipients, and these have translated into improved outcomes. Increased understanding of the pathogenesis of infectious syndromes, introduction of new antimicrobial agents, adoption of empirical antibiotics during aplasia before engraftment, development of novel strategies to prevent and treat infections, and recognition of the contributory role of infectious pathogens to the morbidity of other transplant complications, especially graft-versus-host disease (GVHD), have all been responsible for improved survival rates ***(Thomas, 2009).***

Aim of the work

Review of antimicrobial prophylaxis and methods of prevention of infection in patients with hematopoietic stem cell transplantation

Methods

Review of literature and recent publications, including journals relevant to our study.

Introduction

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Hematopoietic Stem Cell Transplantation

Hematopoietic stem cell transplantation has evolved over more than 50 years of cumulative laboratory observation, animal studies and clinical studies which defined the essentials of transplant biology. A lot of obstacles faced the development of Bone marrow transplantation(BMT) as an established model of therapy, starting from finding the feasibility of intravenous infusion as a route for stem cell transplantation, through methods to overcome the host immune system to allow establishment of the graft, and through the identification of the major histocompatibility complex (MHC) in man and immunosuppressive therapy to overcome the development and the control of graft versus host disease ***(Thomas, 1999).***

Historical background to Hematopoietic Stem Cell Transplantation:

A Danish investigator, Capricious – Moeller, noted that when the legs of guinea pigs were shielded during exposure to total body irradiation (TBI), the usual depression of platelet counts and post irradiation hemorrhagic diathesis was prevented (1926). These important observations were largely ignored or forgotten for 25 years, when in (1951), Jacobson and colleagues rediscovered these observations. They reported that mice exposed to doses of radiation that caused fatal marrow aplasia could be protected from death by shielding of the spleen, a hematopoietic organ in the mouse. With remarkable insight they also showed that protection from lethal effects could be accomplished by the intraperitoneal injection of spleen cells following TBI ***(Schmitz et al.,2002).***

The first successful allogenic bone marrow transplants done worldwide, using HLA identical sibling (simultaneous transplants done in minneaolis by Robert Good, et al., in 1968,) coated from **(*Johnson, 1991 , Thomas, 1999).***