Preparing the Patient for Bone Marrow Transplantation: 
Nursing Care Issues

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The phases of bone marrow transplantation can be identified as the pre-transplant period, the immediate post-transplant period, and the late post-transplant period. The pre-transplant period is characterized by identification of the appropriate type of transplant to be done and, if necessary, finding an appropriate donor; entry of the patient into the transplant unit; administration of the preparative chemotherapy/irradiation regime; management of early toxicities; and pre-transplant supportive care.

Nurses play an integral role during the entire transplant process. During the pre-transplant phase, nursing expertise is exemplified in the administration of chemotherapy, management of side effects, teaching of transplant procedures to patient and family, and supportive care.

This paper reviews the patient care issues during the pre-transplant phase of bone marrow transplantation and identifies nursing management strategies.

The evolution of bone marrow transplantation over the past 25 years has seen it advance from an investigational attempt to salvage patients who had failed all conventional therapies to first-line therapy for a cadre of malignant and non-malignant diseases [1,2,3,4].

Of the malignant disorders, successful transplantation has been achieved in acute lymphocytic leukemia [2,5,6], acute non-lymphocytic leukemia [7,8], chronic myelogenous leukemia [9], Hodgkin’s disease [10], non-Hodgkin’s lymphoma [11], neuroblastoma [12], and selected solid tumors [13].

Increased success rates in the acute and chronic leukemias were due, in part, to using marrow transplantation earlier in the disease process, as with chronic myelogenous leukemia, in stable phase [14,15], and transplantation in remission versus relapse, in the acute leukemia group [16,17,18]. In addition to a lower leukemic cell burden at the time of transplant, these patients were physically, nutritionally, and psychologically stronger and better able to sustain the rigors of the transplant. Today, as the numbers of marrow transplants steadily increase, discussion of its use is often initiated soon after the diagnosis is confirmed and, for some patients, movement toward transplant begins during the initial therapy.

For the non-malignant disorders, bone marrow transplantation is now the treatment of choice for severe combined immunodeficiency disorder [19] and in severe aplastic anemia in children and young adults [20,21].

The congenital and hereditary disorders in which marrow transplantation has been used include Wiscott-Aldrich syndrome [22], juvenile osteopetrosis [23], Gaucher’s

Abbreviations: CMV: cytomegalovirus HLA: human leukocyte antigen LAF: laminar air flow MLC: mixed lymphocyte culture

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disease [24], Diamond-Blackfan syndrome [25], thalassemia [26], and sickle-cell anemia [27].

The early advances in marrow transplantation were directly related to (1) the identification of the human leukocyte antigen (HLA) system, (2) the development of chemotherapy/irradiation combinations which were effective in eradicating disease and in being immunosuppressive enough to allow engraftment of foreign marrow into the host, and (3) the development of intensive support to the patient during the period of profound myelosuppression [3].

Today, continued work is directed at improving the preparative therapy to reduce the risk of relapse, combining more effective immunosuppressive agents to reduce the frequency and severity of graft-versus-host disease, and incorporating new technology in the care and support of patients. In addition, attempts are being made to establish a non-related donor registry which would potentially offer marrow transplantation to a greater number of individuals. As the numbers of survivors of marrow transplantation increase, attention must also be directed at both the long-term physical and psychological effects.

The process of bone marrow transplantation can be separated into three phases: the pre-transplant period, the immediate post-transplant period, and the late post-transplant period. The focus of each phase is distinct, yet each clearly overlaps with one another. The pre-transplant period is characterized by the identification of an appropriate donor, entry of the patient into the transplant unit, administration of the preparative therapy, management of early toxicities, and pre-transplant supportive therapy. The immediate post-transplant period includes the transplant itself, acute complications related to the transplant and/or the chemotherapy/irradiation regime, and post-transplant support during profound pancytopenia and immunosuppression. The late post-transplant period is characterized by preparation for discharge, late complications related to the preparative therapy and/or transplant process, and management of prolonged immunosuppression.

Psychologically, patients, donors, and family also go through phases of coping and adaptation during the process of bone marrow transplantation. These issues will be addressed in a later paper. Nurses play a vital role in the care of the patient undergoing bone marrow transplantation, melding state-of-the-art science with clinical care. It is through the expertise of nurses that the patient does not fall victim to the high technology but rather becomes the beneficiary of such support.

The purpose of this paper is to review patient care issues during the pre-transplant phase. Following papers will examine the immediate post-transplant care and the long-term care of the bone marrow transplant patient.

**PATIENT/DONOR SELECTION**

The first steps in the process of bone marrow transplantation focus on patient and donor selection. Consideration for marrow transplantation is based on the following: (1) that the patient's disease is one which there is a defective or absent element in either the hematopoietic or immune system which can be corrected by transplantation, (2) alternate therapies are limited, (3) the risks of the disease process outweigh the risks of the transplant, and (4) there are no pre-existing conditions which may prevent the patient from surviving the transplant [28].

Donor selection is influenced by the type of transplant to be done. Autologous transplantation occurs when the individual's own marrow is used; thus, donor and
recipient are the same. Syngeneic transplants are those between identical twins. Allogeneic transplantation remains the most widely used type and involves the use of a donor either related or unrelated. Donor selection for allogeneic transplantation is based on tissue compatibility, which is determined through human leukocyte antigen (HLA)/mixed lymphocyte culture (MLC) typing. Each individual possesses a unique combination of HLA antigens, of which half are inherited from each parent. The probability of two siblings inheriting the same HLA antigens is approximately 30 percent [29]. Once it has been determined that a potential donor matches at the major HLA loci (A, B, C, DR), the D locus is identified by means of mixed lymphocyte culture (MLC). This response looks for mutual non-reactivity between host and donor lymphocytes [30]. HLA tissue typing is essential, therefore, in predicting potential for graft rejection and graft-versus-host disease in the marrow transplant recipients [30].

Peripheral blood is obtained from the patient and all members of the immediate family. Results of the HLA/MLC determinations may take as much as two weeks. For the patient and family, not knowing whether there is, in fact, a donor produces a great deal of anxiety and a mixture of conflicting feelings. The patient may alternate between feeling hope for a cure and fear of potential consequences of the transplant. For the family, there is anticipation as to who the donor will be and personalization of the impending procedure. Donors may feel that they are responsible for the outcome of the transplant, be it a success or a failure.

ABO typing is also a part of the screening process; however, major incompatibility between the donor and the recipient is not an exclusionary criterion in marrow transplantation. Several studies have shown no significant effect of ABO incompatibility on either occurrence of graft rejection or graft-versus-host disease [31,32]. For major incompatibility, several techniques are utilized to remove antibodies from the recipient in order to prevent hemolysis, including large-volume plasma exchange and immunoabsorption [33,34]. Similarly, removal of erythrocytes from the donor marrow prior to transplantation has resulted in successful engraftment [35].

Procedures to remove incompatible antibodies are initiated for several days prior to the day of the marrow transplant. Intentional incompatible transfusion of donor-type red cells may be administered the night before transplant in order to absorb any remaining antibody and to predict the potential for an acute hemolytic reaction during the infusion of donor bone marrow.

Cytomegalovirus (CMV) antibody status is an issue addressed during the pre-transplant period. CMV infection in transplant recipients is a serious and life-threatening complication. Serology of both the donor and the recipient may affect the development of infection in the post-transplant period. When the patient and/or the donor are seropositive at the time of transplant, CMV infection represents either a reactivation of latent virus in the patient or transmission of another strain of cytomegalovirus from donor to host. When both the patient and the donor are seronegative, transmission of CMV can occur through the administration of blood products which are positive for CMV [33,36]. It is for this reason that CMV-negative blood products are routinely used in the setting where both patient and donor are antibody-negative. No clear benefit for use of CMV-negative products has been established when either the patient or the donor is antibody-positive [36].

Providing CMV-negative blood products is costly and time-consuming. Careful and judicious use of these products is crucial. Nursing responsibilities include assessment of the patient to determine the need for transfusions, cross checking for appropriate blood
products, safe administration of the product, and monitoring patient responses. Preliminary studies using leukocyte removal filters are showing effective removal of CMV from seropositive products with no increased incidence of CMV infection [37]. Clearly, if efficacious, this process could influence transfusion practices in transplantation.

**PATIENT ENTRY INTO TRANSPLANT UNIT**

Once a suitable donor has been identified, the next step in the pre-transplant period is admission of the patient in order to begin the preparative conditioning therapy. The physical environment and the degree of isolation can be addressed from a physical as well as a psychological perspective. The degree of isolation may vary from sole use of a private room to the extreme of laminar air flow isolation and strict sterile technique. In addition to isolation, many centers utilize skin and gastrointestinal decontamination with non-absorbable antibiotics in order to reduce the frequency of severe infections during the time of profound pancytopenia [38]. Studies have shown laminar air flow (LAF) isolation accompanied by the use of non-absorbable antibiotics to be effective in decreasing exogenous infections in patients with acute leukemia and in marrow transplant recipients [38,39,40].

Peterson et al. showed that the use of prophylactic systemic antibiotics with LAF isolation significantly decreased infections when compared to LAF isolation alone [41]. Moreover, in patients with aplastic anemia who undergo allogeneic transplantation in protective environments, there is a decreased frequency and a delayed onset of acute graft-versus-host disease [42]. This finding has not been demonstrated in other marrow transplant populations, such as those with malignant disease.

Emotionally, for the patient, entry into isolation confirms the intensity of the process and marks a point of no return. Stressors of protective isolation include loss of control, lack of physical contact, sleep deprivation, regimented care, and restricted activity [38,43]. Resulting psychological effects of these stressors may include regressive behavior, anxiety over minor procedures, depression, sleep disturbances, excessive demands on staff and family, and noncompliance. Understanding the emotional responses to isolation is an essential component of the nursing care. Holland et al. reported that improved psychological adjustment over time to extreme isolation was due, in part, to the specialized and supportive nursing care given to these patients [44].

Providing the patient and family with the opportunity to visit the unit and to speak with other patients who have experienced isolation may be beneficial in decreasing anxiety and dispelling preconceived images. Patients adapt better to the isolation when educated as to the rationale for its use and the importance to its adherence [44]. It is not unusual for patients to become fearful of leaving their protective isolation when it is time to re-enter the "real world." Nursing provides an easier transition through comprehensive discharge teaching and follow-up care in the outpatient setting.

**PREPARATIVE THERAPY**

For many patients, the preparative chemotherapy/irradiation is not unfamiliar. More often than not, patients have undergone some prior therapy to treat the pre-existing disease and will come to the transplant with some understanding of the drugs, administration techniques, and potential side effects. Exceptions include persons with newly diagnosed severe aplastic anemia and chronic myelogenous leukemia in stable phase. For these patients, admission for marrow transplantation may be their first exposure to hospitalization and intensive therapy.
The rationale for pre-transplant conditioning therapy is based on the need for (1) ablation of the host immune system to allow engraftment of donor cells, (2) effective destruction of residual tumor cells, and (3) sufficient space in the bone marrow cavity [45,46]. The choice of the preparative therapy is determined by the underlying disorder. For malignant disease, it is necessary to eradicate tumor cells in addition to establishing sustained immunosuppression, whereas, for non-malignant disorders, the preparative therapy is directed at immunosuppression alone [46,48].

Typically, chemotherapeutic agents such as cyclophosphamide, busulfan, carmustine, cytosine arabinoside, and etoposide are used alone or in combination to achieve ablative immunosuppression and cytotoxic activity. In the setting of malignant disease, total-body irradiation in doses of 1,000–1,400 rads is delivered in fractionated doses to achieve additional cell kill [45,48]. Delivery of the conditioning chemotherapy is accomplished through central venous catheters, and administration is completed over four to seven days. Total-body irradiation, if indicated, is delivered in daily or twice daily doses over four to seven days prior to the transplant [45,47].

The sequelae of ablative chemotherapy and total-body irradiation begin during administration and continue throughout the phases of marrow transplantation. Many of the long-term complications following bone marrow transplantation are directly related to the preparative therapy administered months earlier [49]. The development of cataracts, restrictive and obstructive lung disease, and growth retardation in children are but a few examples.

Nursing expertise in the administration of chemotherapy and in the prevention and control of side effects is paramount during this period. Knowledge of the fact that many toxicities will occur simultaneously and that the management of one toxicity may exacerbate another creates a high standard for careful and thorough assessment and appropriate interventions [50].

The high doses of chemotherapy and total-body irradiation are clearly toxic to the bone marrow, resulting in loss of hematopoiesis. Other tissues subject to severe toxicity include the gastrointestinal tract, mucous membranes, bladder, central nervous system, lungs, and liver [51].

Gastrointestinal side effects are often the first to appear during administration of the preparative therapy and present a challenge in terms of control and management. The control of nausea and vomiting and the prevention of intractable states can be accomplished with antiemetic therapy. Knowledge of the emetic effects of the agents used and patients' prior experience are necessary in choosing an appropriate agent for antiemetic coverage [52]. Adequate dosing and around-the-clock administration will maintain effective control.

The development of mucositis is, to some degree, almost universal in marrow transplant recipients. Typically, breakdown of the mucous membranes begins simultaneously with a dropping white count, involves the oropharynx, and may extend to the esophagus [51]. Aggravation of the mucositis occurs with progressive xerostomia, increased acidic saliva, bacterial or fungal superinfections, and pre-existing dental pathology [53]. Reactivation of herpes simplex infection frequently occurs in the presence of mucositis [51,53], and prophylactic treatment with acyclovir may be useful in reducing the severity of the mucositis [54]. Rarely, mucositis may cause airway obstruction, resulting in the need for intubation or tracheostomy [51]. Mucositis is more often self-limiting, resolving within weeks, occurring concurrently with early engraftment. Management focuses on meticulous oral care to remove debris, preven-
tion of superinfection, and relief of pain. Pain management usually requires systemic analgesia, with continuous morphine being the most effective agent [53].

High doses of cyclophosphamide carry the risk of bladder toxicity in the form of hemorrhagic cystitis, which may develop during administration or may be delayed weeks or months [51]. Symptoms include dysuria, frequency, frank hematuria, and clot formation [51]. Methods to reduce the frequency of hemorrhagic cystitis include the use of a three-way Foley catheter with large-volume irrigation [47] and, more recently, the systemic infusion of mercaptoethanol sulphonate sodium concurrently with the cytoxan [55].

Early toxicity of total-body irradiation includes nausea, vomiting, diarrhea, fever, alopecia, and parotiditis. When such irradiation is given concurrently with chemotherapy, the toxicities of either modality may be magnified.

PRE-TRANSPLANT TRANSFUSION SUPPORT

Transfusion practices during the pre-transplant period should reflect judicious use of blood products to decrease sensitization and alloimmunization. Transfusion-induced graft rejection has been most clearly documented in patients with aplastic anemia [33]. Rejection rates were more pronounced when transfusions were from the intended donor compared with random non-related donors. This finding has resulted in practices which avoid using all family members as donors for blood products during the preparative period. Additional measures include the use of leukocyte-poor, filtered, or frozen deglycerolized products.

A final transfusion practice, that of irradiation of all blood products, begins at the time of the preparative therapy and continues for the lifetime of the patient. This procedure is done to prevent transfusion-induced graft-versus-host disease by eliminating immunocompetent T lymphocytes in the blood products.

CONCLUSION

The pre-transplant period marks the entrance of the patient into a lifelong process of care. Nursing is an integral member of the multidisciplinary team who care for the bone marrow transplant patient. The pre-transplant period is intensive for the delivery of the preparative therapy, management of early complications, and teaching and support to the patient and family. Culmination of this period occurs on the day of the marrow transplant, and the focus of care then shifts to address a whole new group of potential problems.

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