High-Dose Chemotherapy With Autologous Stem Cell Rescue in the Outpatient Setting

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The number of autologous peripheral blood progenitor cell (PBPC) transplants performed annually has increased dramatically over the past decade. Autologous PBPC transplants have quickly moved from the exclusive province of the academic medical center to part of the armamentarium of the practicing community oncologist.

Three technical developments have facilitated the widespread application of this technology in the community setting. First, increased familiarity with standardized conditioning regimens has made the toxicity of high-dose chemotherapy predictable.[1] Second, the use of cytokine-mobilized peripheral blood stem cells (PBSCs) that contain larger numbers of CD34+ cells, compared to bone marrow autologous grafts, has shortened the period of post-transplant neutropenia.[2,3] Third, the development of effective, standard supportive care measures for the transplant maneuver has permitted patients to be managed in the outpatient setting throughout the administration of their conditioning regimen, as well as during the post-transplant recovery phase.

Economic Forces That Support Outpatient Transplants

The article by Dix and Geller reviews the technical advances and logistic infrastructure in supportive care that have helped make outpatient transplants possible. Clinical outcomes related to the complications of transplantation appear to be similar when comparing inpatient and outpatient transplant models.[4] A major impetus for the shift toward outpatient transplants is economic—transplant centers negotiate with third-party insurers for global “case-rate” contracts that pay a fixed reimbursement for the transplant procedure.[5] The increasing number of academic and private practice centers that offer transplant services has increased competition for these contracts, leading to decreases in the reimbursement that the transplant center receives from third-party insurers.

In order to decrease the cost of caring for patients in the hospital during the transplant maneuver, transplant centers have adapted by delivering some, or all, of their care in the outpatient setting. Successful transplant centers have integrated care across inpatient, outpatient, and in-home settings to preserve optimal clinical outcomes while reducing hospital days. The challenge for the next decade will be to find the appropriate “mix” of these different care settings.

The article by Dix and Geller describes three models of outpatient care. In the “early discharge” model, patients are discharged from the inpatient setting at the completion of high-dose chemotherapy. In the “delayed admission” model, patients receive both high-dose conditioning chemotherapy and the autologous transplant in the outpatient setting. Patients are admitted to the hospital if they develop significant mucositis, enteritis, or neutropenic fever. In the “comprehensive outpatient” model championed by the authors, patients are supported throughout the entire transplant maneuver in the outpatient setting. Each model has resulted in decreased hospitalization rates and median lengths of stay, as compared with historical cohorts of patients transplanted and supported throughout the period of neutropenia in the hospital setting.[4,6]

The economic consequences of the comprehensive outpatient care model are best illustrated in the authors’ Figure 3. In traditional hospital-based transplant models, 75% of the total revenue from managed care contracts went to the hospital, with 25% of the revenue supporting the costs of outpatient care—a reflection of the relative distribution of resources across inpatient and outpatient settings.[4] In the model described by Dix and Geller, hospital charges for inpatient care comprised only 4% of the total cost, with all hospital-related charges comprising only 20% of the total. In a study by Rizzo et al, 17 patients undergoing a transplant incurred only 29% of their charges in an
inpatient facility.[4] The comprehensive outpatient care model thus represents a shift of revenue from the hospital inpatient service to outpatient clinics, practitioners, pharmacies, and laboratories. While the total cost of the autologous transplant maneuver remains approximately $30,000 to $60,000,[6-8] revenue in the comprehensive outpatient care model mainly supports the payment of the transplant team salaries, outpatient pharmacy, home health care personnel, and outpatient facilities. The transplant center assumes control over cost and revenue distribution, as opposed to directing most of the clinical revenue to the inpatient facility. As a result, the transplant center is able to efficiently allocate resources to provide the personnel needed to ensure that patients remain safe while recovering from neutropenia, mucositis, and enteritis as outpatients.

Of note, in the model described by Dix and Geller, transplant nurses expend a significant amount of effort to maintain contact with patients through telephone calls and by initiating and coordinating home health care services that are not directly reimbursable, yet are critical to maintaining positive clinical outcomes and patient satisfaction.

**Potential Disadvantages of Outpatient Transplant Models**

Although the comprehensive outpatient care model has advantages from the standpoint of decreasing overall resource utilization and efficiently integrating clinical care across inpatient and outpatient settings, this approach does have inherent disadvantages. Some patients may prefer to stay at home during much, if not all, of the transplant maneuver. However, many patients do not live within the requisite 30-minute driving radius of the transplant center, and must stay in local hotels during their outpatient transplant, thus mitigating the advantage of remaining in their own domicile during the transplant.

In addition, patients may spend much of their day in the clinic receiving treatment or undergoing various diagnostic tests. For example, for the outpatient, the administration of high-dose conditioning therapy may require an appointment lasting more than 12 hours, thereby limiting the relative advantage to staying at home during this phase of the transplant maneuver. The patient and caregiver must also get to and from the clinic, as well as to the laboratories performing various diagnostic tests.

Thus, the outpatient transplant models shift a significant amount of responsibility for management of complications of high-dose therapy and autologous PBPC transplantation onto the patient and caregiver(s). This cost shifting may have a significant economic impact on the patient and caregiver that is difficult to measure.[4,9]

Another significant limitation to outpatient care models is the management of enteritis and mucositis in the conditioning and immediate post-transplant phase. The article by Dix and Geller describes the management of nausea and vomiting using a combination of granisetron (Kytril) and dexamethasone and a patient-controlled patient-activated intermittent (BAD) pump that delivers regulated doses of a mixture of Benadryl, Ativan, and dexamethasone during the conditioning regimen. Analogous to patient-controlled analgesia, by using the BAD pump, patients can anticipate and treat nausea before it leads to significant emesis. The future use of new agents, such as keratinocyte growth factor,[10] may further decrease the enteral toxicity related to the conditioning regimen, thus further reducing the need to hospitalize patients for significant mucositis and enteritis.

**Outpatient Allogeneic Transplants**

The future of autologous transplantation is firmly placed in the outpatient setting. The comprehensive outpatient care model described by Dix and Geller represents the practical integration of many incremental advances in supportive care that have been made over the past decade. A challenge for the future will be whether a similar approach can be generally applied to the management of patients undergoing allogeneic transplantation.

In general, the mucosal toxicity of total-body irradiation, coupled with the post-transplant administration of methotrexate, has required significant amounts of parenteral narcotics for pain control, as well as parenteral nutrition. With new allogeneic transplant strategies employing megadoses of donor hematopoietic progenitor cells[11] and avoiding the need for post-transplant immunosuppression,[12] full outpatient allogeneic transplants are becoming feasible.

However, the cost savings that are achieved for high-risk patients undergoing outpatient transplantation most likely will be modest, due to the probability of hospital admissions for treatment-related complications.[4] Such an outpatient approach to allogeneic transplantation will require a redoubling of staff resources to help manage patients who are at risk for life-threatening opportunistic infections and graft vs host disease, which is not generally seen in autologous transplant recipients.

Whether it is safe for neutropenic, allogeneic transplant recipients to be maintained outside of a
relatively protected, high-efficiency particulate air (HEPA)-filtered environment remains unclear. The successful management of allogeneic transplant recipients in the outpatient setting will ultimately require new strategies to enhance immune reconstitution in these patients.

References:


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