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ALLOGENEIC STEM CELL TRANSPLANTATION USING HIGH-DOSE CYTARABINE COMBINED WITH G-SCF AND TBI AS CONDITIONING FOR CHRONIC MYELOGENOURS LEUKEMIA (CML) IN ADVANCED STAGE

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The outcome of allogeneic hematopoietic stem cell transplantation (allo-HSCT) for CML in advanced stages (accelerated phase (AP) and blast crisis (BC)) is extremely poor, although allo-HSCT remains as the only curative treatment. We have evaluated the efficacy of the conditioning consisting of high-dose cytarabine (HDCA) combined with continuous infusion of G-CSF and TBI. The addition of G-CSF to HDAC was based on the hypothesis that G-CSF may increase the susceptibility of leukemic cells to cytarabine. [PATIENTS & METHODS] 13 patients with CML in advanced stages (AP=6, BC=7) received the conditioning and all were evaluable. Median age at transplant was 39 (range: 22-51). 10 patients received unrelated BM, 2 patients received related PBSC, and one patient received unrelated CB as a source of stem cells. Conditioning included TBI (2Gyx6) followed by HDCA alone (n=6) or with cychophosphamide (120mg/kg, n=7). HDCA was administered at a dose of 2-3g/m2 x4 or x8 doses together with continuous infusion of G-CSF (5mcg/kg) starting 12 hours before HDCA and continuing until starting final dose of HDCA. GVHD prophylaxis was short-term MTX with cyclosporine A for related transplant (n=3) or with FK506 for unrelated transplant (n=10). [RESUTLS] As regiment related toxicities, mucositis and conjunctivitis were frequent in patients receiving HDCA 3g/m2 x 8 doses. One died of bacterial infection before engraftment. Engraftment was obtained in 12 patients. 7 of 12 patients developed in acute GVHD (grades >II), and 8 of 11 evaluable patients developed chronic GVHD. With the median follow-up of 16 months, 3-year overall survival and disease-free survival were 60% and 54.7%, respectively. 7 patients are still alive and in molecular remission. Causes of death included extensive chronic GVHD (n=2), liver failure (n=1), Pneumocystis carinii pneumonia (n=1), bacterial infection (n=1), and leukemia relapse (n=1). [CONCOLUSION] HDCA together with continuous infusion of G-CSF in combination with TBI as conditioning may improve the outcome of allo-HSCT for CML in advanced stages.

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REDUCED-INTENSITY CONDITIONING STEM CELL TRANSPLANT (RIC-SCT) WITH FLUDARABINE/BUSULFAN/ATG FOR HEMATOPOIETIC MALIGNANCIES

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Historically, conditioning regimens for allogeneic SCTs are associated with significant regimen-related toxicity (RRT) especially in patients with advanced age, prior treatment, and underlying comorbidities. RIC regimens have been shown to allow engraftment with decreased RRT. We studied RIC regimens in twenty-four patients (median age 54 years; range 21-66). Diseases treated were ALL (1), AML (7), CLL (2), CML (2), MDS (2), MM (6), and NHL (4). Fifteen patients received stem cells from matched sibling donors (MSD), 2 patients from a 1-antigen mismatched sibling, and 7 patients from matched-unrelated donors (MUD). Eight patients had received previous SCT. The RIC regimens consisted of either fludarabine 40mg/m^2/d (n=8) or fludarabine 25 mg/m^2/d IV (n=16) x 5 doses, busulfan 1mg/kg/dose PO x 8 doses, and horse (n=23) 10 mg/kg/d or rabbit-derived (n=1) 1.5 mg/kg/d antithymocyte globulin x 4 doses. GVHD prophylaxis consisted of tacrolimus 0.03 mg/kg/d CIV starting on day -2 and methotrexate 5 mg/m^2 IVP on days 1, 3, and 6. The median number of CD34$^+$ cells transplanted was 8.0 x 10^6/kg. Median time to neutrophil engraftment was 18 days (range 14-31 days). Donor chimerism was established in 88% of patients at day 100, and 82% of evaluable patients had greater than 90% donor chimerism at 1 year. The incidence of grade II or higher RRT was 12.5% (3 pts), and there was one toxic death attributed to fludarabine (40 mg/m^2) toxicity. The 100-day transplant-related mortality was 14% (3 pts). Grade II or greater aGVHD developed in 24% (5) of evaluable patients, while 80% (12) developed cGVHD (extensive=10). Actuarial estimate of disease-free survival at 12 months was 84% (10 pts). These RIC regimens allowed adequate engraftment with decreased RRT, however, GVHD, relapse, and infectious complications caused significant morbidity and mortality.

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IMPROVING TRANSPLANT REVENUE MANAGEMENT IN A MULTI-HOSPITAL TRANSPLANT ENTERPRISE

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The Health Alliance of Greater Cincinnati is a six hospital system with three hospitals providing transplant services. The Health Alliance was not capturing reimbursement potential in transplant billing and collection. A Transplant Revenue Process Improvement Team of 15 people was formed including representation from administration levels of solid organ and BMT programs, Payor Relations, Patient Accounting, Financial Coordinators, Registration and Organizational Effectiveness. From July 2001-September 2001 this group spent over 24 meeting hours and 100 work hours studying current processes, determining areas of opportunity and making recommendations. Four recommendations were made: 1) Create a specialized position, Transplant Operations Analyst (TOA) to manage all patient/donor accounts. 2) Create an integrated database from the three existing transplant databases allowing the TOA to remain apprised of all new patients. 3) Create/implement transplant-specific identification cards for patients and donors in order to register them correctly. 4) Create a Transplant Underpayment Recovery Unit to review all underpaid transplants for the past 18 months. Results: A second TOA position was needed. The database was enhanced to track other costs and allow the TOA to report on any transplant population at any time. The ID cards are invaluable in the tracking process. Of the initial $5,112,433 in underpaid claims, over $4,200,000 was collected (118% of the original goal of $3,570,000). There are only 261 organ transplant hospitals among the over 5,000 acute care hospitals in the US placing organ transplant hospitals in a highly specialized area. The disciplined approach to transplant revenue management processes and the significant collaboration of the multidisciplinary transplant business team has positively affected the bottom line.

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MEDI-TRANSPLANTATION AFTER INTERMEDIATE INTENSITY OF BU (12MG) /CY (120MG) CONDITIONING REGIMEN

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Non-myeloablative Stem Cell Transplantation (NST) has lower morbidity and mortality when compared with transplantation following conventional conditioning with Bu (16mg) /Cy (120mg) regimen. However, quick relapse and /or fast disease progression following NST is often a concern for aggressive diseases such as poor prognostic Leukemia, MDS and high grade lymphoma. In an attempt to reduce toxicity yet at the same time to preserve the dose-intensity, we have reduced the dose of busulfan to 12 mg/kg from 16 mg/kg in combination with 120 mg/kg cyclophosphamide (Medi-transplant regimen) for patients with AML in advanced relapse and/or with poor prognostic features. Cyclosporine and Mycophenolate were used for GVHD prophylaxis. 6 patients (age 27-53) with AML (3 in 2nd refractory relapse, 2 in 2nd CR, one first cytogenetic relapse with Ph+ chromosome) underwent the medi-transplantation. Three were sibling donors, two were matched-unrelated graft, another was 5/6 unrelated graft. All 6 engrafted promptly with full donor chimerism at engraftment. Mild acute GVHD was seen in related transplants, severe GVHD was seen in the unrelated grafts. Overall, acute complications are less severe. Engraftment with full donor chimerism for both related and unrelated grafts were readily achievable.