Fetal Liver Cytokines : Potential Therapeutic Value

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Abstract

Due to the paucity of lymphoid cells, weak expression of HLA antigens, higher proliferative potential as well as higher long term repopulating ability of fetal liver cells compared to adult bone marrow (BM) and the minimal potential to induce graft versus host disease (GvHD), fetal liver cells (FLC) have been utilized to treat severe combined immune deficiency, aplastic anemia and other disorders. Of the 41 patients of aplastic anemia infused with FLC by us, 40% demonstrated slow and incomplete autologous hematopoietic recovery. Stable engraftment was not demonstrable as the preconditioning regimen was not utilized. To dissect the role of fetal liver infusion (FLI) in autologous hematopoietic recovery, the colony supporting potential of fetal liver conditioned medium (FLCM) was evaluated in BM cells of normal adult and aplastic anemia patients. In both cases, each sample of FLCM supported the growth of colony supporting cells in semisolid culture medium. The FLCM was analyzed for the presence of colony stimulating cytokines namely stem cell factor (SCF), Granulocyte macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL-3), erythropoietin (EPO), IL-6 and FLt-3. GM- CSF and IL-3 were absent in most FLCM samples. EPO in small quantity was present in 30% of samples. SCF was present in more than 50% of samples. Flt-3 and IL-6 were present in majority in more than 80% of the samples. Bioneutralization assay confirmed 42% suppression of CFU-GEMM colonies with the addition of anti SCF antibody to FLCM. Suppression was 42% with anti IL-6 and 20% with anti Flt-3 antibody. Using RT-PCR method gene expression for SCF, GMCSF, Epo, IL-6 and Flt-3 was demonstrable. Suitable combination of cytokines may be a useful management strategy for the treatment of aplastic anemia.

Keywords: lymphoid cells, fetal liver cells, cytokines, aplastic anemia, hematopoiesis