SHORT COMMUNICATION

Granulocyte Transfusion in Children

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We describe a single institution experience with the use of granulocyte transfusion in children. This is a retrospective analysis of 45 collections of granulocyte units obtained by apheresis after priming with dexamethasone, infused into 17 children with severe neutropenic infections. Ten children survived the acute infection. Granulocyte transfusion is a useful adjunct to antimicrobials and growth factors in post chemotherapy neutropenic sepsis and is highly effective in children with chronic granulomatous disease and life threatening infections.

***Keywords**: Granulocyte transfusion, Neutropenia, Sepsis.*

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Children undergoing intensive chemotherapy for malignant diseases, stem cell transplantation and with granulocyte function disorders are at increased risk of neutropenia. Neutropenia is the single most important reason for the development of severe bacterial and fungal infections in immunocompromised children, contributing to both morbidity and mortality(1-3). Transfusion of neutrophils in such children appears a logical option(4-6). Trials have suggested that granulocyte transfusions are bene-ficial as an adjunct to the ongoing therapy(7-9). The present study is a single institution retrospective analysis of granulocyte transfusions in children.

METHODS

The study was done in the Pediatric Intensive Care Unit and Hematology unit of Apollo Hospitals, Chennai. Forty five transfusions were done in the five year period between March 2002 and March 2007 in 17 children. The ethics committee of Apollo Hospitals Chennai approved the protocol for granulocyte transfusion in sick children. Informed consent was taken from all parents and the donors before the donation and transfusion of granulocytes.

Granulocyte donors were healthy relatives or voluntary donors, who were tested for ABO and RhD compatibility(10). Donors were informed regarding the apheresis technique and that participation would include administration of steroids prior to the procedure. Granulocyte colony stimulating factor was not used in priming donors. All the donors were screened for HIV, Hepatitis B and C, malaria and syphilis. They were given 8 mg of dexamethasone orally with 40 mg of pantoprazole approximately 8-12 hours before the apheresis.

Granulocytes were collected by centrifugation leucaphersesis (COBE Spectra). Approximately 8-10 liters of blood was processed in 120 minutes using peripheral venous access. The collected granulocyte units were maintained at room temperature, were irradiated with 25 Gy and used within six hours of collection.

The recipients included children with granulocyte function disorders or those with absolute neutrophil count of <500/cu mm and severe bacterial or fungal sepsis resistant to ongoing antimicrobial therapy and growth factors. Resolving infection, absence of fever for more than 24 hours and improvement in neutropenia were considered as endpoints for granulocyte transfusion.

Granulocytes were transfused over a period of 1-2 hours with monitoring of vital parameters. Premedication consisted of 15mg/kg of acetaminophen, 4mg/kg of hydrocortisone and 0.1 mg/kg of chlorpheniramine maleate. In children who had received amphotericin B for treatment of fungal infection, granulocytes were transfused at least 4-6 hours prior to or after its administration.

RESULTS

Seventeen children received granulocyte transfusions. The profile of these children is depicted in ***Table* I**. Two children developed transient pulmonary reactions with escalation of ventilatory requirements and decrements in oxygenation levels on day 3 and day 2, respectively, after receiving granulocytes.

Of 17 children, 10 were boys. The age of included subjects ranged from 18 months to 16 years (median 8 years; IQR 4-12 years). Overall, 10 children survived. Two of the expired children had refractory neutropenia. Days of neutropenia ranged from 2-37 d in the rest of the subjects. Number of units of granulocytes transfused ranged from 1 to 10 (median 2; IQR 1-4).

DISCUSSION

With the advent of newer apheresis techniques and better priming of the donor, the yield of granulocytes has been superior. We did not employ the use of G-CSF in priming of the donors, as the yield with steroids was adequate for use in children. Cytomegalovirus (CMV) screening was not done, as over 90% of our donors are CMV positive anyway. We did not encounter CMV transmission in any of

TABLE I PROFILE OF CHILDREN WHO RECEIVED GRANULOCYTE TRANSFUSIONS

Underlying disease	Granulocyte per unit counts	Infection profile/cultures	Days of neutropenia
CGD	2.6×10^9	Liver abscesses, *Candida kruseii, Klebsiella*	7
CGD	3.82×10^9	*Staph.aureus, Citrobacter, Candida albicans*	12
Kostmann's syndrome	2.5×10^9	Necrotising fasciitis of anterior abdominal wall, *Candida albicans*	refractory
ALL–T cell	2.6×10^9	Invasive Aspergillosis	refractory
ALL–T cell	5.3×10^9	*E.coli,* non-fermenting gram negative bacilli, aspergillosis	20
AML-M2 (MDS)	2.1×10^9	*Candida parapsilosis, Klebsiella, S. aureus*	2
AML-M6 (MDS)	1.29×10^9	MRSA	3
AML-M2	2.1×10^9	*Pseudomonas,* Enterococci	10
AML-M4	1.9×10^9	*Pseudomonas,* Aspergillosis/Candida	15
Severe aplastic anaemia, Dyskeratosis congenita	2.1×10^9	*E.coli,* Aspergillosis	15
Neuroblastoma-post peripheral stem cell transplantation	2.1×10^9	*Candida geulermondi*	16
ALL PH+	4.9×10^9	*Pseudomonas sepsis* with cardiomyopathy	20
Bilineage leukaemia	Not available	Enterococcal sepsis	21
Severe aplastic anaemia post ATG	Not available	No positive cultures	15
Non Hodgkins Lymphoma	0.91×10^9	No positive cultures	15
Severe aplastic anaemia post BMT	Not available	Pseudomonas with icthyma	37
HLH	3.5×10^9	Enterococcal sepsis	11

ALL – acute lymphoblastic leukemia; AML – acute myeloblastic leukemia; BMT – bone marrow transplantation; ATG – antithymocyte globulin; HLH – Hodgkin's lymphoma; PH: philadelphia

our immunocompromised recipients. All the units were irradiated to prevent graft versus host disease in the recipients.

To the best of our knowledge, this is first report from India focusing on the emerging role of the use of granulocyte transfusion in the management of critically ill children. We conclude that granulocyte transfusions have a role in reducing the duration of infection and hence reducing the mortality in children with refractory neutropenic sepsis. The combination of steroids and granulocyte colony stimulating factor would have increased our yield of granulocytes several fold. We hope to study the efficacy of the two drug mobilizing regimen in our next protocol.

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