A study report of 174 units of placental umbilical cord whole blood transfusion in 62 patients as a rich source of fetal hemoglobin supply in different indications of blood transfusion

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Summary

Background: In the animal kingdom, even herbivorous animals swallow the placenta after the birth of the baby (for example, the cow). In the human system, we do not know about the proper utilization of the placenta and membranes although there are suggestions regarding this on the basis of research on placental umbilical cord blood stem cells as an alternative to bone marrow transplantation. In this present series of placental umbilical cord whole blood transfusions, we wanted to examine the safety aspect of other components of cord blood transfusion, e.g., fetal RBC, growth factors and cytokine filled plasma, etc., in different indications of blood transfusion, from the pediatric to the geriatric age group, in malignant and non-malignant disorders affecting our patients.

Methods: One hundred and seventy-four units of umbilical cord whole blood were collected aseptically from the umbilical vein after caesarean section in standard pediatric blood transfusion bags*, after the removal of the baby from the operative field and after confirming the stable condition of the mother. The volume of cord blood varied from 50 ml to 140 ml with a mean of 86 ml ± 16 ml.

Results and Analysis: The cord blood was transfused immediately (within three days of collection) to 62 patients from nine years to 78 years of age, of whom 32 were suffering from varying stages and grades of malignancy from 1 April 1999 till date i.e., 11 Aug 2000, after obtaining adequate consent and following the precautions of standard blood transfusion protocol. The remaining 30 patients included patients suffering from thalassemia major, aplastic anemia, systemic lupus erythematosus, chronic renal failure, rheumatoid arthritis, ankylosing spondylitis and a geriatric group of patients with benign prostatic hypertrophy. All have tolerated the procedure without any immunological or non-immunological reactions.

Conclusion: On the basis of our experience with 174 units of placental umbilical cord whole blood transfusion in malignant and non-malignant conditions (within three days of collection and preservation at 1-6°C in a refrigerator), we are of the opinion that this is a safe transfusion protocol which takes advantage of the safety of nature's finest biological sieve, i.e., the placenta, as an alternative to adult whole blood transfusion. It also has the advantage of a higher oxygen carrying capacity of fetal hemoglobin in addition to many growth factors and other cytokine filled cord blood plasma along with its hypoantigenicity.

Key words: Fetal hemoglobin; Placental umbilical cord whole blood; Safe transfusion.

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* Pediatric blood bags contain 14 ml anticoagulant-citrate phosphate dextrose adenine solution USP and a 16 g needle for transfusion.

Introduction

The use of umbilical cord blood stem cells as an alternative to bone marrow transplantation has aroused global interest because it is (a) less expensive, (b) easily available and (c) has a low graft *vs* host reaction, since the first publication of the stem cell transplant report [1-7]. However, the use of other constituents of umbilical cord whole blood has not been properly studied so far although there is an existing global discrepancy in the demand and supply of available fresh whole blood for immediate transfusion.

The present project was undertaken to examine the efficacy and safety of placental umbilical cord whole blood transfusion as an alternative to standard adult whole blood transfusion with the necessary informed consent and strictly following the ethical committee's guidance for the project.

Materials and Methods

One hundred and seventy-four units of umbilical cord whole blood was collected after lower uterine caesarean section. Only after the baby was safely removed from the operative field and the mother was verified to be in stable physical condition, was the decision to proceed with umbilical cord whole blood collection taken. The cord was disinfected with Betadine solution and the needle attached to a standard pediatric collection bag was introduced into the umbilical vein. The blood flowed by gravity and generally stopped within two mintues. When the collection was complete, the blood bag tubing was closed and sealed and stored at 1-6°C after necessary identification markings. Another small sample of cord blood was taken separately for ABO/RH grouping [8], Australia antigen [9] by EIA Kit (supplied by Omega Diagnostics, UK), hepatitis C [10] by EIA Kit Detect HCV (supplied by Biochem Immunosystems Inc., Montreal, Canada) HIV 1 and 2 [11] by EIA Kit Detect HIV (supplied by Biochem Immunosystems Inc., Montreal, Canada) and malaria, as per standard protocol of blood transfusion practice.

The collected blood volume varied from 50 ml to 140 ml (mean 86 ml ± 16 ml) and it was preserved in refrigerators and transfused (within three days of collection) to different patients with ages varying from nine years to 78 years. Before the umbilical cord blood transfusion, a thorough clinical examination of the recipient was done including monitoring of BP/pulse/respiration and other cardinal features. Then 5 ml of blood was drawn to assess the routine Hb/Tc/Dc/ESR/platelet, Coombs test [12], C reactive protein [13], urea [14], creatinine [15], bilirubin [16] and subsequently blood was redrawn after 24 hours, 72 hours, 7 days, one month, two months, and three months from the transfusion to see if there was any adverse reaction and to study the effects of transfusion.

After necessary cross-matching of the specimens and double checking the patient's identity, cord blood was given through an appropriate administration set containing a filter (230 um) via a careful aseptic technique. For the initial 15 minutes after the start of the infusion, the patient was observed for any sign of transfusion reaction. Thereafter, if all went well, the infusion rate was increased until the transfusion was completed.

Result and Analysis

Between 1 April 1999 and 30 March 2000, 89 units of cord blood were collected and transfused to 20 patients suffering from different malignant tumors and 12 other cases suffering from non-neoplastic conditions. From 1 April 2000 up to date (11 August 2000), 85 units of cord blood were transfused to 14 patients suffering from malignant diseases and another 16 suffering from non-malignant conditions (see Table).

Out of 62 cases that received whole cord blood transfusions up to date, the highest transfusion of 15 units was provided to a stage IV cancer patient (serial no. 35), then 10 units to two cases (serial nos. 1 and 10), then 9 units (serial nos. 18 and 19), 8 units (serial no. 4), 6 units (serial nos. 6, 13 and 32), 5 units (serial nos. 2, 20, 27, 37 and 45). Patients with ankylosing spondylitis, thalassemia major and autoimmune diseases like systemic lupus erythomatosus, rheumatoid arthritis, and aplastic anemia also received cord whole blood without any side-effects. It is interesting to note that patients with chronic renal failure and geriatric patients suffering from benign prostatic hypertrophy, etc., tolerated this infusion of cord whole blood without the slightest clinical problem, without leaving any scope for the utilization of a support system like O_2 inhalation, predehydration with frusemide, etc., even at a Hb content as low as 4 g percent, though all support systems were kept ready as stand-by.

Discussion and Conclusion

The blood volume of a term infant is approximately 80-85 ml/kg [17-20]. The placental vessel at term contains approximately 150 ml of blood [21]. The cord blood contains three types of hemoglobin, HbF, HbA and HbA_2. HbF constitutes the major fraction (50-85%) [22]. HbA accounts for 15 to 40% of the hemoglobin and HbA_2 is present only in trace amounts (0.3%) at birth [23]. HbF has a greater affinity for oxygen than HbA [24]. The oxygen tension at which the hemoglobin of cord blood is 50% saturated (P_{50}) is 19-20 mm Hg., 6-8 mm Hg lower than that of normal adult blood. This shift to the left of the hemoglobin oxygen disolution curve results from poor binding of 2,3 diphosphoglycerate by HbF [25, 26].

The potential complications of blood transfusion therapy can be grossly classified as (a) immunological and (b) non-immunological [27]. The immunological reactions are related to the stimulation of antibody production by foreign allo antigens by different components of the transfusion, e.g. RBC, leucocyte, platelet, plasma proteins. Allo-immunization may lead to immunological reactions in case of future stimulation by a similar antigen.

The commonly encountered immunological reactions are haemolytic reactions due to red cell compatibility, febrile or pulmonary reactions related to antigens of lucocutes or platelets, allergic anaphylactoid reactions related to antibodies and very rarely graft *vs* host reaction due to engraftment of the transfused lymphocytes in case of immunosuppression.

The commonly encountered *non-immunological* reactions are related to the physical and chemical properties of the transfused blood/blood products due to bacterial or viral contamination and circulatory load.

Table. — *Summary of the clinical presentation of the recipients of umbilical cord whole blood.*

Pt. no.	Name, age & sex	Blood group	Primary diagnosis	Transfusion of UCBT	Immediate reaction	Late reaction	Overall clinical condition	Other treatment
1	AC 35 yrs. F	A+	Ca-Breast Stage II	10 Units 1st 23.4.99 Last 13.6.00	Nil	Nil	Very good	Modified radical mastectomy followed by radiotherapy and chemotherapy
2	BS 54 yrs. M	A+	Fibre Sarcoma Stage IV and diabetes	5 Units 1st 25.4.99 Last 1.8.99	Nil	Nil	Poor	Polychemotherapy (adriamycin vincristine and bleomycin) 2 units of whole blood transfusion
3	SB 65 yrs. M	B+	Ca-Tonsil Stage II	1 Unit 12.5.99	Nil	Nil	Good	Postsurgery, postradiotherapy
4	AP 16 yrs. M	B+	Non Hodgkins lymphoma Stage IV	8 Units 1st 11.5.99 Last 13.7.00	Nil	Nil	On 9/99 GC was good. Discontinued treatment and admitted in 5/00 with very poor GC	Chemotherapy (endoxan, vincristine and prednisolone)
5	GG 42 yrs. F	B+	Ca-Breast Stage III	2 Units 1st 17.5.99 Last 22.5.99	Nil	Nil	Poor	Postradiation and CMF chemotherapy (cyclophophomide, 5-flurourocil).
6	GB 35 yrs. M	O+	Ankylosing spondylitis	6 Units 1st 30.5.99 Last 21.8.99	Nil	Nil	Good	Steroid and methotrexate, analgesics and physiotherapy and vitamins
7	KD 40 yrs. F	A+	Ca-Breast Stage IV	1 Unit 23.6.99	Nil	Nil	Good	CMF chemotherapy (cyclophosphomide metrotrexate, 5-flurourocil)
8	SD 30 yrs. F	B+	Ca-Breast Stage IV	2 Units 1st 4.8.99 Last 6.12.99	Nil	Nil	Good	Radiation and chemotherapy CMF (cyclophosphomide, methotrexate, 5-flurourocil)
9	TKM 24 yrs. M	A+	Thalassemia major	1 Unit 8.8.99	Nil	Nil	Moderately good	Blood transfusion + folic acid + desferrol injection
10	UB 30 yrs. F	B+	Ca-Breast II	10 Units 1st 12.8.99 Last 19.6.00	Nil	Nil	Very good	Surgery followed by radiotherapy followed by chemotherapy CMF (cyclophosphomide, methotrexate, 5-flurourocil)
11	GB 71 yrs. M	O+	Benign hypertrophied prostate	1 Unit 21.8.99	Nil	Nil	Good	Transurethral resection
12	SR 18 yrs. F	AB+	Osteomylitis foot	1 Unit 21.8.99	Nil	Nil	Good	Antibiotics (ofloxacin)
13	AG 78 yrs. F	O+	Ca-Larynx Stage IV	6 Units 1st 28.8.99 Last 21.2.00	Nil	Nil	Poor	Chemotherapy methotrexate, vincristine, bleomycin, epirubicin
14	GD 75 yrs. M	O+	Benign prostate hypertrophied	1 Unit 31.8.99	Nil	Nil	Poor	Catheterisation and supportive treatment
15	AD 30 yrs. F	O+	Arthritis with deformity	4 Units 1st 18.2.99 Last 12.9.99	Nil	Nil	Good	Non steroidal anti-inflammatory drugs + methotrexate + physiotherapy
16	MS 24 yrs. M	B+	Anemia with bone marrow depression	2 Units 1st 7.9.99 Last 25.9.99	Nil	Nil	Good	supportive treatment
17	SMD 60 yrs. M	AB+	Ca-Prostate	1 Unit 12.9.99	Nil	Nil	Poor	Oestrogen and supportive treatment and catheterisation
18	AD 45 yrs. F	B+	Ca-Cervix Stage II	9 Units 1st 16.9.99 Last 24.7.00	Nil	Nil	Poor	Wartheim surgery followed by radiation
19	SK 55 yrs. F	A+	Ca-Colon Stage IV	9 Units 1st 30.9.99 Last 31.5.00	Nil	Nil	Moderately good	Chemotherapy with 5-fluorouracil and leucovorin rescue
20	BDG 50 yrs. F	B+	Ca-Breast Stage II	5 Units 1st 3.10.99 Last 3.1.00	Nil	Nil	Good	Modified radical mastectomy and radiation
21	AM 60 yrs. F	AB+	Calcaneal #	1 Unit 25.11.99	Nil	Nil	Good	Supportive treatment and immobilisation
22	PB 55 yrs. M	A+	Ca-Breast Stage IV	1 Unit 27.1.00	Nil	Nil	Good	Chemotherapy on 19.1.00 (CMF) Cyclophosphomide, methotrexate and 5-fluorouracil

Table (cont.) — *Summary of the clinical presentation of the recipients of umbilical cord whole blood.*

Pt. no.	Name, age & sex	Blood group	Primary diagnosis	Transfusion of UCBT	Immediate reaction	Late reaction	Overall clinical condition	Other treatment
23	SC 45 yrs. F	B+	Leucoplakia-Vulva	2 Units 1st 8.2.00 Last 8.2.00	Nil	Nil	Good	Supportive treatment after excision therapy
24	JM 60 yrs. F	B+	Prolapse-Uterus	1 Unit 11.2.00	Nil	Nil	Good	Ward Mayo operation
25	BRB 69 yrs. F	B+	Severe anemia with splenomegaly	1 Unit 12.2.00	Nil	Nil	Good	Supportive treatment
26	EC 52 yrs. F	O+	Ca-Ovary with metastasis to lung and liver	2 Units 1st 13.2.00 Last 21.2.00	Nil	Nil	Very poor	Received 10 units of whole blood Platelet concentrate and supportive hyperalimentation
27	MK 45 yrs. M	O+	Osteo sarcoma-Right Hand	5 Units 1st 18.2.00 Last 27.6.00	Nil	Nil	Good	Recurrence treated with second high level amputation and chemotherapy. methotrexate and vincristine
28	AS 50 yrs. M	AB+	Thymoma	1 Unit 8.3.00	Nil	Nil	Poor	Radiation and high dosage of prednisolone and supportive drugs
29	SD 50 yrs. F	AB+	Ca-Ovary Stage IV	2 Units 1st 14.3.00 Last 18.4.00	Nil	Nil	Good	Chemotherapy with cisplatinum methotrexate, bleomycin + supportive treatment
30	PR 55 yrs. F	A+	Ca-Cervix Stage IV	2 Units 1st 18.4.00 Last 17.5.00	Nil	Nil	Good	Palliative surgery to control bleeding + supportive treatment
31	BC 62 yrs. M	A+	Bleeding P/R	1 Unit 20.4.00	Nil	Nil	Good	Surgery for infected prolapsed piles
32	KJ 32 yrs. F	A+	Osteo sarcoma-Leg	6 Units 1st 20.4.00 Last 27.6.00	Nil	Nil	Good	Sauserisation and iliac crest bone chips support followed by chemotherapy with Vincristine, epirubicin and methotrexate
33	AR 26 yrs. F	A+	S.L.E. (systemic lupus erythematosus)	1 Unit 15.3.00	Nil	Nil	Good	Methotrexate and supportive treatment
34	SK 37 yrs. M	O+	Ca-Penis Stage II	1 Unit 27.3.00	Nil	Nil	Good	Chemotherapy after amputation of penis with methotrexate, cisplatinum and vincristine
35	DCS 51 yrs. M	O+	Metastatic neck gland-Stage IV	15 Units 1st 28.11.99 Last	Nil	Nil	Poor	Radiation and chemotherapy with 5-fluorouracil and leucovorin rescue
36	RPS 46 yrs. M	AB+	Ca-Stomach Stage IV	1 Unit 7.4.00	Nil	Nil	Poor	5-fluorouracil and leucovorin rescue
37	NKG 53 yrs. M	B+	Bronchogenic Ca Stage IV	5 Units 1st 13.4.00 Last 9.5.00	Nil	Nil	Poor	Etoposide, bleomycin, adriamycin with supportive drugs
38	SG 60 yrs. M	B+	Ca-Prostate Stage IV	1 Unit 25.4.00	Nil	Nil	Poor	Oestrogen and catheterisation and supportive drugs
39	UP 35 yrs. F	B+	Ca-Cervix Stage IV	1 Unit 14.5.00	Nil	Nil	Poor	Radiation and supportive treatment
40	AM 72 yrs. M	O+	Benign hypertrophy of prostate	1 Unit 17.5.00	Nil	Nil	Good	Prostatectomy
41	AH 60 yrs. M	O+	Pylonic stenosis	1 Unit 28.5.00	Nil	Nil	Good	Gastrojejunostomy and H_2 blocker support
42	RDS 40 yrs. F	O+	Bronchiectasis	1 Unit 28.5.00	Nil	Nil	Good	Supportive treatment and adult whole blood transfusion
43	SD 50 yrs. F	O+	Intestinal tuberculosis	1 Unit 31.5.00	Nil	Nil	Good	Rifampicin, INH myambutal, pyrazinamide and supportive drugs
44	KD 28 yrs. F	A+	Severe anemia	2 Units 1st 7.6.00 Last 12.6.00	Nil	Nil	Good	Supportive haematinics
45	MB 42 yrs. M	O+	Ca-Lung with bone metastasis Stage IV	5 Units 1st 22.6.00 Last	Nil	Nil	Poor	BCG and supportive drugs for pain relief
46	AB 28 yrs. F	O+	Bleeding P/R in the background of cirrhosis	2 Units 1st 22.6.00 Last 27.6.00	Nil	Nil	Good	Cirrhosis liver support treatment

Table (cont.) — *Summary of the clinical presentation of the recipients of umbilical cord whole blood.*

Pt. no.	Name, age & sex	Blood group	Primary diagnosis	Transfusion of UCBT	Immediate reaction	Late reaction	Overall clinical condition	Other treatment
47	LKM 66 yrs F	AB+	Adenocarci--noma-Uterus	3 Units 1st 7.8.00 Last	Nil	Nil	Good	Radical hysterectomy
48	KNH 47 yrs F	O+	Recurrent peptic ulcer with peptic perforation	4 Units 1st 1.7.00 Last 23.7.00	Nil	Nil	Good	Repair of peptic perforation followed by metranidazol + Clarithromycin, omeprazol and supportive drugs
49	RCC 53 yrs. M	B+	Ca-Tongue Stage II	1 Unit 2.7.00	Nil	Nil	Good	Hemiglossectomy followed by radiation and supportive treatment
50	MD 17 yrs. F	O+	Neurocysticer-cosis	1 Unit 11.7.00	Nil	Nil	Good	Albendazol + supportive drugs
51	SF 27 yrs. F	O+	Appendicitis	1 Unit 12.7.00	Nil	Nil	Good	Appendectomy
52	RD 47 yrs. F	A+	Severe anemia & diabetes & Chronic renal failure	3 Units 1st 11.7.00 Last 26.7.00	Nil	Nil	Good	Supportive treatment for chronic renal failure and human actrapid insulin injection and Inj. Erythropoietin
53	LP 17 yrs. F	AB+	Severe anemia	2 Units 1st 17.7.00 Last 2.8.00	Nil	Nil	Good	Haematinics
54	NGD 57 yrs.M	B+	Cholelithiasis	1 Unit 17.7.00	Nil	Nil	Good	Cholecystectomy
55	RD 15 yrs. F	O+	Rheumatoid arthritis and irregular fever	1 Unit 8.7.00	Nil	Nil	Good	Steroid & non steroidal anti-inflamatory drugs and supportive treatment
56	RC 45 yrs. F	O+	Ca-Breast Stage II	2 Units 1st 14.7.00 Last 17.7.00	Nil	Nil	Good	Modified radical mastectomy on 14.7.00
57	SD 47 yrs. F	A+	Bronchogenic carcinoma Stage II	1 Unit 17.7.00	Nil	Nil	Poor	Chemotherapy with cyclophosphomide etoposide methotrexate, 5-fluorouracil
58	PC 78 yrs. M	B+	Ca-Tongue Stage II	1 Unit 19.7.00	Nil	Nil	Moderately good	Hemiglossectomy and chemotherapy with bleomycin, vincristine and methotrexate
59	AG 35 yrs. F	B+	Tumor-(Rt.) breast	1 Unit 23.7.00	Nil	Nil	Good	Removal of fibroadenoma
60	SD 45 yrs. M	A+	Ca-Lung Stage IV with poor GC	1 Unit 2.8.00	Nil	Nil	Good	Patient refused chemotherapy. Supportive therapy
61	KD 9 yrs. F	A+	Thalassemia major	1 Unit 7.8.00	Nil	Nil	Good	1 bottle of blood transfusion and folic acid and Inj. desferrol
62	AG 47 yrs. F	AB+	Thalassemia Minor with acute appendicitis	1 Unit 9.8.00	Nil	Nil	Good	Appendectomy

Fetal hemoglobin carries 20-50% more oxygen than the mother's blood. Moreover, there is the advantage of the Bohr effect of fetal hemoglobin by which it can carry more oxygen at low PCO_2 than at high PCO_2 [28]. These are all additional advantages of cord blood transfusion. In addition, the cord blood plasma contains many growth factors in the cytokine system. In a subsequent publication, we will give information on the degree of engraftment of the stem cell (CD_{34}) and also CD_4, CD_8 ratio, etc., from the peripheral blood sequential immunophenotype study of the recipients of the cord whole blood. We are also working on the fate of HbF and other hemoglobins like A/A2/F/C/S/D through a sequential Hb electrophoresis study after the transfusion of cord whole blood.

On the basis of our experience with 174 units of placental umbilical cord whole blood transfusion since 1 April 1999, we can see that such transfusion of placental whole blood, after following the standard blood transfusion protocol, can be safely used in case of need of blood transfusion from the pediatric to the geriatric age groups, as an alternative to the transfusion of adult whole blood – not as an inferior method of transfusion but as an effective supplementation of blood without any transfusion related problems.

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