206

Autologous Cord Blood Stem Cells as A Treatment for Neonates with Hypoxic Ischemic Encephalopathy (HIE): Stability and Safety of Autologous Cord Blood Stem Cells by Transport

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Background:
Hypoxic-ischemic encephalopathy (HIE) is considered a major cause of cerebral palsy (CP) in moderately or severely asphyxiated newborns. Until now, therapeutic hypothermia (TH) for HIE has been the only effective treatment to prevent the onset of CP. We conducted a phase I trial of TH and autologous cord blood stem cell therapy in six patients with HIE to confirm its safety and feasibility. (Table1)

Objective:
To verify the stability and safety of the transport of cord blood and cord blood stem cell preparations necessary for treatment.

Methods:
Cord blood samples were transported for a test run at 6-10° C for approximately 5 hours. Cells were isolated by SEPAX2, CD34 was measured by flow cytometry, and cell number and viability were determined. Bacterial contamination was confirmed by Gram staining, and the cell solution was prepared for transport after isolation. The isolated cord blood stem cell preparations were also tested for quality by performing a test run at 6-10° C for approximately 5 hours, as was the case with cord blood.

Results:
1. Transport of cord blood for approximately 5 hours at 6-10° C had no particular effect on the number of viable cells, recovery rate, or CD34 viability before and after land transfer. (Fig. 1)
2. Transport of cord blood stem cell preparations for approximately 5 hours at 6-10° C had no particular effect on the number of viable cells, suvival rate, or CD34 viability before and after land transfer. (Fig. 2)

Conclusions:
The stability and safety of the land transport of cord blood and cord blood stem cell preparations required for the treatment was confirmed, and it was thought that autologous cord blood stem cell therapy for HIE could be implemented at more medical institutions.

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Table 1. Six patients with HIE treated by autologous cord blood stem cell.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
GA	38gw1d	40gw0d	41gw4d	39gw5d	38gw5d	39gw5d
BW(g)	2436	2507	3024	4086	2723	2723
AP score	2/5	0/0	2/2	5/6	2/7	1/3
Remarks	Abruption	Cord prolapse	Mother CPA	Obstructed Labor	Malrotation Obstructed Labor	Mother SAH
ABG(pH)	7.2	6.9	7.1	7.2	7.1	7.0
Base deficit	7.4	20	9	5.1	10	7.0
Sarnat	II	III	II	II	II	II
Thompson	15	12	9	12	15	9
CA	4Y0m	3Y7m	3yY3m	2Y9m	2Y5m	1Y8m
DQ (Age)	88 (1Y6m)	-	-	110 (1Y6m)	109 (1Y6m)	95 (6m)
ADL	ADHD	Tube feeding	spastic	normal	normal	normal
Brain MRI (Age)	n.p. (1M)	abnormal (32D)	abnormal (1M)	n.p. (10D, 1Y)	n.p. (10D,1Y)	n.p. (30D)

(Tsuji M, et al. Sci Rep. 2020 Mar 12;10(1):4603.)

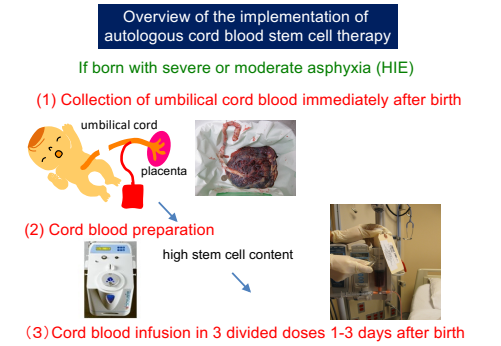
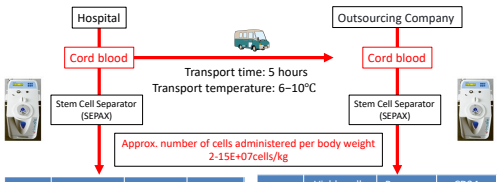


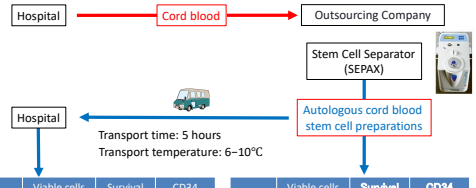
Fig. 1. Effects of cord blood transport



	Viable cells (cells)	Recovery rate (%)	CD34 Viability (%)
Bag 1	8.28E+08	81	99.7
Bag 2	2.88E+08	92	100
Bag 3	7.96E+08	67	99.6
Mean	6.37E+08	81	99.8

	Viable cells (cells)	Recovery rate (%)	CD34 Viability (%)
Bag 1	3.51E+08	78.0	98.0
Bag 2	1.22E+08	75.8	98.8
Bag 3	4.75E+08	82.5	92.2
Mean	3.16E+08	79.2	95.5

Fig.2. Stability of autologous cord blood stem cell preparations



	Viable cells (cell/mL)	Survival rate (%)	CD34 Viability (%)
Bag 1	1.985.E+07	97.20	94.910
Bag 2	1.675.E+07	96.80	90.825
Bag 3	2.285.E+07	96.35	91.495
Mean	1.980.E+07	96.8	92.41

	Viable cells (cell/mL)	Survival rate (%)	CD34 Viability (%)
Bag 1	1.880.E+07	97.55	93.350
Bag 2	1.775.E+07	98.80	94.410
Bag 3	2.140.E+07	95.85	93.580
Mean	1.930.E+07	97.4	93.78