"Quality Issues with Umbilical Cord Blood for Transplant"

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Introduction

- Cord blood banking has moved from the R & D stage into standardized product.
- Cord blood now licensed by FDA.
- Major effort to build National Cord Bank Inventory.
- Quality of cord blood is important.
- 10 years ago, we found quality issues in large proportion of units.
- To determine progress, we repeated the study of quality of cord blood units.

Methods

- Used quality system developed for general cell therapy laboratory.

- Includes:
  - Standardized process for reviewing all aspects of cell products shipped for transplant

- All cord blood units received for transplant 2011-2013 reviewed using quality system.

- Issues were grouped as: medical history, quality control/assurance (QC), and labeling and documentation.

Methods (cont.)

- Medical history issues further classified as: maternal medical/social, extended family, paternal, and miscellaneous.

- QC issues categorized as: transmissible disease testing, microbiology, temperature monitoring, processing methods, and miscellaneous.

- Labelling issues categorized as labeling or paper work.

- All quality issues were categorized as: likely (L), potential (P), or unlikely (U) to have adverse clinical impact.

Bank	Number of UCB units received	Number of UCB units with issues	Number of issues	Frequency of UCB units with issues (%)	Mean numbers of issues/ UCB unit
Cord Blood banks from which units with quality issues were received.					
USA					
1	54	36	50	67	1.4
2	40	25	41	63	1.6
3	36	27	42	75	1.6
4	30	13	16	43	1.2
5	25	12	21	48	1.8
6	13	8	13	62	1.6
7	12	8	9	67	1.1
8	10	9	17	90	1.9
9	9	8	17	89	2.1
10	7	6	9	86	1.5
11	5	2	2	40	1.0
12	3	1	2	33	2.0
13	1	1	1	100	3.0
14	1	1	3	100	3.0
Europe					
15	1	1	1	100	1.0
16	2	1	1	50	1.0
Total	**249**	**159**	**245**	**64**	**1.5**

Category and potential patient impact of quality issues: 2011-2013 in comparison to 2001-2003.

2011-2013					2001-2003				
		Potential impact					Potential impact		
Category	Total number (%)	Likely	Potential	Unlikely	Category	Total number (%)	Likely	Potential	Unlikely
Medical History	117 (48)	1	45	71	Medical History	99 (40)	4	37	58
QC	120 (49)	2	80	38	QC	132 (54)	18	37	77
Labeling & documentation	8 (3)	4	4	0	Labeling & documentation	15 (6)	4	11	0
Total	245 (100)	7	129	109	Total	246 (100)	26	85	135

Quality Issues Related to Maternal Medical or Social History

			2011-2013	2001-2003	
			# (%)	# (%)	Quality Impact
Maternal medical and/or social history			**49 (20)**	**36 (15)**	**P**
Recent travel outside of US (e.g. France, Italy)			28	17	P
Living outside US (e.g. England, Germany)			11	3	P
Use of donor sperm			1	2	P
Navel piercing, tattoos(s) acupuncture			1	6	P
History of malaria or Lyme disease			1	2	L
History of herpes			4	2	U
History of chlamydia			1	1	U
Sex with HIV-positive father of baby			0	1	NA
Possible hematologic abnormalities			1	6	P

Quality Issues Related to Maternal Medical or Social History (cont.)

	2011-2013	2001-2003	
	# (%)	# (%)	Quality Impact
Extended family medical history and/or disease	**46 (19)**	**42 (19)**	
Cancer			
Blood	3	5	U
Non-blood	25	31	U
Others (e.g. ALS, Addison's, SLE, RA)	18	6	U
Paternal Social History	2 (1)	4 (1)	
Risk Factors (intravenous drug use, HIV+)	0	2	NA
Adopted- limited family history	2	2	P
History of low platelet count	0	2	NA
Miscellaneous maternal medical issues	**20 (8)**	**11 (4)**	U
Total issues related to medical history	**117 (48)**	**99 (40)**	

Issues in the QC Results

	2011-2013	2001-2003	
	# (%)	# (%)	Quality Impact
Transmissible disease testing	**27 (11)**	**21 (9)**	
Incomplete	20	13	
- HIV/HCV NAT tested outside of manufacturers instructions	20	--	P
Pending	1	1	P
Positive results	**0**	**7**	NA
Inconsistent reporting of infectious disease testing	6	--	P

Issues in the QC Results (cont.)

	2011-2013		2001-2003		
	#	(%)	#	(%)	
Microbiology	**46**	**(19)**	**89**	**(36)**	
Positive culture	**2**		4		L
Maternal Group B Streptococcal colonization	14		20		U
Peripartum admin. of antibiotics or antivirals	18		31		U
Elevated maternal temp	4		2		U
Prematurely ruptured membranes (range 15-31 hr)	2		11		U
Primary bag break or leak at time of thaw	**6**		**8**		P

Issues in the QC Results (cont.)

	2011-2013	2001-2003	
	# (%)	# (%)	Quality Impact
Temperature indicator	**10 (4)**	**7 (3)**	
Cryoguard color in question	--	2	NA
Logger data inadequate	8	--	P
Placement of probe questioned	2	--	P
Absent – shipper in alarm mode	0	5	NA

Issues in the QC Results (cont.)

	2011-2013		2001-2003		
	# (%)		# (%)		Quality Impact
Miscellaneous issues related to UCB unit	**37 (15)**		**11 (4)**		
>20% nucleated RBC count	7		5		P
<50% viability	1		2		P
Poor CFU growth	7		2		P
Leaking segment	2		1		P
Confirmatory HLA testing needed, segment available	16		--		P
Confirmatory HLA testing needed, segment available	4		--		P
Total QC issues	**120 (49)**		**132 (54)**		

Labeling & Documentation Issues

Category		2011-2013		2001-2003		Quality Impact
		Number	*(%)*	*Number*	*(%)*	
UCB unit labeling		2	(1)	8	(3)	
	Incomplete	1		6		P
	Mislabeled	1		2		L
Paperwork accompanying UCB		6	(2)	7	(3)	
	Incomplete	3		5		P
	Mislabeled	3		2		L
	Total	**8**	**(3)**	**15**	**(6)**	

Relationship of quality issues to engraftment problems

Engraftment Problem	Number of UCB transplants	Quality issues per transplant event				# CB units	Quality issues per unit			
		No	%	Yes	%		No	%	Yes	%
2011- 2013	n=173					n= 249				
No	154	41	**27**	113	**73**	227	83	**37**	144	**63**
Yes	16	4	**25**	12	**75**	19	7	**37**	12	**63**
Not evaluable	3	1	33	2	67	3	1	33	2	67
2001- 2003	n=194					n=268				
No	162	45	**28**	117	**72**	221	84	**38**	137	**62**
Yes	32	9	**28**	23	**72**	47	16	**34**	31	**66**

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Number of Issues in Umbilical Cord Units by Years Banked (2001-2012) and infused between 2011-2013

Years Banked	# Units	# Units with issues	# Issues	Average # Issues/ Units with Issues	Average #Issues/ Total Units
2001-2003	4	4	6	1.50	1.50
2004-2006	31	28	47	1.68	1.52
2007-2009	108	66	102	1.55	0.94
2010-2012	106	61	90	1.48	0.85
Total	249	159	245	1.54	0.98

Conclusions

- Overall number of quality issues unchanged from previous 10 years.
- Issues per unit decreased approximately 36%.
- Most recently:
  - Higher proportion of medical history and lower proportion of QC and labelling/documentation issues.
  - Lower proportion of issues likely to have clinical impact.
  - Most medical history issues unlikely to have clinical impact.
  - Substantial improvement in transmissible disease testing and reports
  - Many QC issues remain and some are quite concerning.
  - Although labelling/documentation issues decreased by about 50%, some still quite concerning.
- Quality issues identified here were not associated with engraftment problems.
- Recommend renewed discussion of value of many donor selection requirements.