

Effectiveness of G-CSF in Hospitalized Infants

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Background

- Neutropenia is common in hospitalized infants
- Granulocyte-colony stimulating factor (G-CSF) is approved for treatment of neutropenia in cancer patients and for patients with chronic severe neutropenia
- G-CSF has been used to prevent sepsis in infants with neutropenia and as adjunctive therapy for infants with sepsis-related neutropenia
- Use of G-CSF in infants is controversial due to conflicting efficacy data

Objective

- Determine if G-CSF use is associated with improved outcomes in neutropenic hospitalized infants

Methods

- We identified all infants with neutropenia during the first 120 days of life in 348 neonatal intensive care units (NICUs) managed by the Pediatric Medial Group between 1997-2012
- Primary outcome: death or secondary sepsis at 14 and 28 days
- Secondary outcomes:
 - Death at 14 and 28 days
 - Secondary sepsis at 14 and 28 days
 - Time to hematologic recovery
- Definitions:
 - Neutropenic episode: ≥ 1 day with an absolute neutrophil count (ANC) of $\leq 1500/\mu\text{L}$
 - Start day: first day of G-CSF in treated group and first day of neutropenia in untreated group
 - G-CSF treated neutropenia: use of G-CSF 2 days before or after the first day of neutropenia
 - Time to hematologic recovery: number of days from the start of neutropenia to the first day with an ANC $> 1500/\mu\text{L}$
 - Concurrent bacteremia: positive blood culture obtained within 2 days before or after the start day
 - Secondary sepsis: a positive blood culture with new organism from days 3-28 after the start day
- Association between G-CSF use and death or secondary sepsis was determined using logistic regression controlling for:
 - Gestational age, small for gestational age, ventilator use and inotropic support and concurrent bacteremia
- Time to hematologic recovery was determined using Cox regression stratified by gestational age and adjusted for: small for gestational age status, inotropic support, mechanical ventilation and concurrent bacteremia

Results

- We identified 30,705 infants with neutropenia, 2142 (7%) treated with G-CSF (Table 1)
- Time to hematologic recovery was shorter for infants treated with G-CSF treatment, hazard ratio 1.36 (95% confidence interval 1.30, 1.44) (Figure 1)
- The odds of sepsis, death and the composite outcome were increased for infants treated with G-CSF at 14 and 28 days (Table 2)

Table 1. Patient Demographics

	G-CSF N=2142 (%)	No G-CSF N=28,563 (%)
Gestational age, weeks, median (25, 75%tile)	28 (26, 31)	29 (27, 32)
Birth weight, grams, median (25, 75%tile)	935 (655, 1451)	1173 (820, 1720)
Male	61	59
Cesarean section	73	72
Maternal hypertension*	17	15
Small for gestational age	33	21
Inotropic support on start day	30	12
Ventilator support on start day	47	45
Concurrent bacteremia	6	4

*Maternal hypertension includes preeclampsia, eclampsia and hemolysis, elevated liver transaminases, low platelet (HELLP) syndrome

Results

Figure 1. Time to hematologic recovery for neutropenic infants, days.

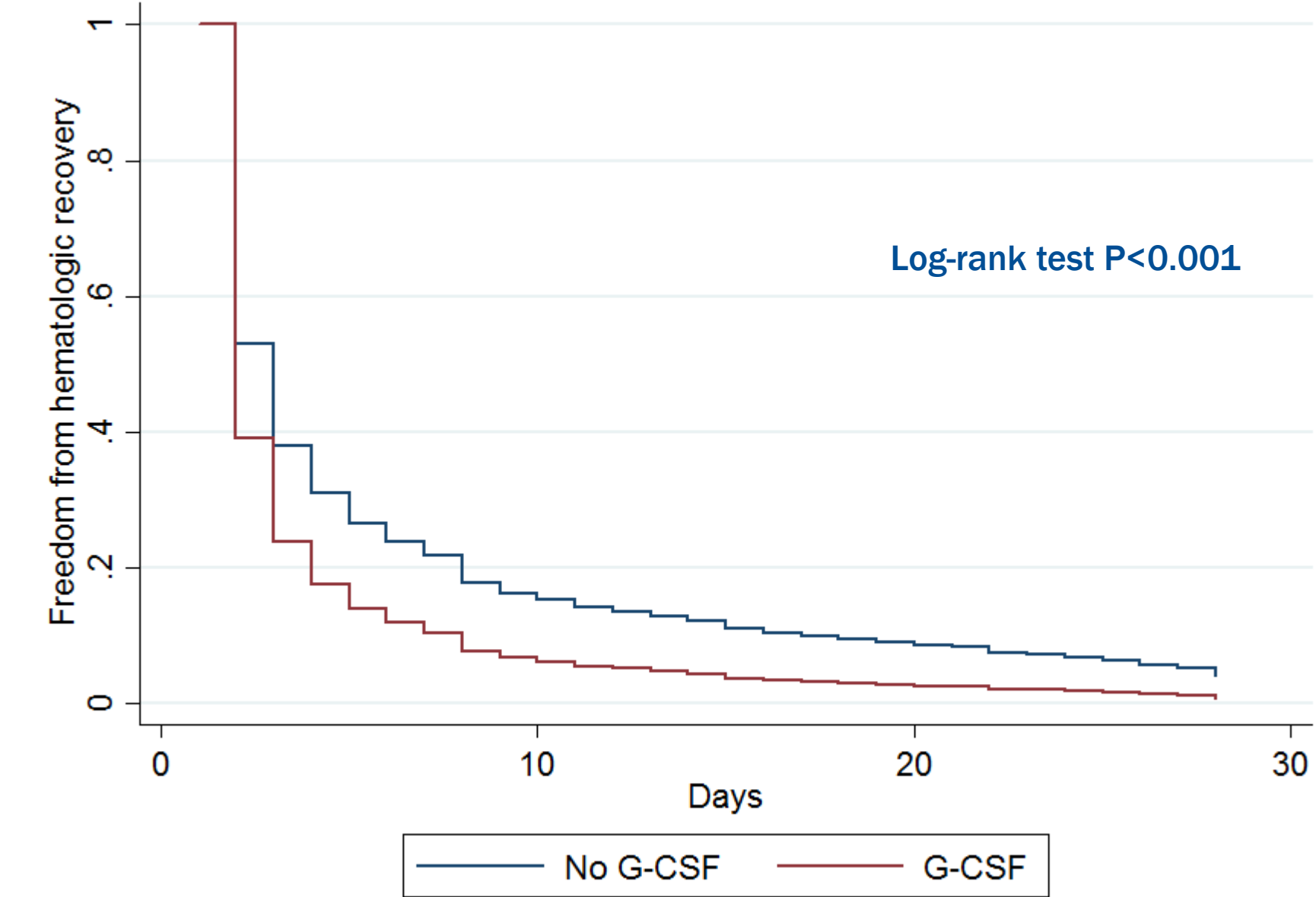


Table 2. Outcomes

	G-CSF N=2142 (%)	No G-CSF N=28,563 (%)	Adjusted Odds Ratio* (95% confidence interval)
Death or Secondary Sepsis			
14 days	235 (11)	1779 (6)	1.50 (1.20, 1.87)
28 days	321 (15)	2712 (9)	1.31 (1.09, 1.57)
Death			
14 days	124 (6)	776 (3)	1.33 (1.05, 1.68)
28 days	157 (7)	1073 (4)	1.32 (1.07, 1.62)
Secondary Sepsis			
14 days	127 (6)	1072 (4)	1.41 (1.19, 1.67)
28 days	192 (9)	1772 (6)	1.29 (1.10, 1.50)

*Odds of outcome for G-CSF group compared to non-G-CSF group adjusted for gestational age at birth, postnatal age, small for gestational age status, inotropic support, ventilator support and concurrent bacteremia.

Conclusions

- G-CSF treatment reduces the time to hematologic recovery but appears to increase mortality and secondary sepsis in treated infants. Caution is needed with G-CSF use in neutropenic infants.



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