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Dose Requirement, Injection Burden, and Cost Implications of Darbepoetin Alfa Versus Recombinant Erythropoietin Beta in Children With CKD-Related Anemia

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ABSTRACT

Introduction: Anemia is a common complication of chronic kidney disease (CKD) in children. Although darbepoetin alfa offers the advantage of less frequent dosing compared with recombinant human erythropoietin beta (rHuEPO beta), evidence regarding its effectiveness and safety in the pediatric population remains limited. **Aim of the study:** Anemia is a common complication of chronic kidney disease (CKD) in children. Although darbepoetin alfa offers the advantage of less frequent dosing compared with recombinant human erythropoietin beta (rHuEPO beta), evidence regarding its effectiveness and safety in the pediatric population remains limited. **Methods & Materials:** This multicenter, open-label, randomized controlled study was conducted in two pediatric nephrology centers in Dhaka, Bangladesh, from October 2019 to September 2020. Children aged 1 to 18 years with CKD-related anemia, including dialysis-independent CKD stages G3b to G5 and dialysis-dependent CKD G5d, were randomized to receive darbepoetin alfa or rHuEPO beta. Darbepoetin alfa was administered subcutaneously at 0.75 µg/kg/week with extended dosing intervals according to dialysis status, while rHuEPO beta was administered subcutaneously at 100 IU/kg three times weekly. The intention-to-treat (ITT) cohort included 44 children, and the per-protocol (PP) cohort included 33 children. **Results:** Darbepoetin alfa required fewer injections than rHuEPO beta, with a markedly lower monthly injection burden. Monthly darbepoetin alfa dose remained stable throughout the early treatment period, whereas the monthly rHuEPO beta dose increased. At 16 weeks, hemoglobin response was comparable between the treatment groups. At 48 weeks, the PP analysis demonstrated a higher mean hemoglobin level with darbepoetin alfa. Injection-site pain was reported more frequently with darbepoetin alfa, whereas the frequency of hypertension was similar between groups. **Conclusion:** Darbepoetin alfa provided a reduction in injection regimen while still having similar efficacy on the hemoglobin levels compared with those children with anemia caused by chronic kidney disease. Although the drug showed a better efficacy profile, further multicenter studies are still necessary.

Keyword: *Chronic kidney disease, Pediatric anemia, Darbepoetin alfa.*

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INTRODUCTION

Anemia is a common and clinically significant complication of chronic kidney disease (CKD) in children, particularly among those with advanced non-dialysis-dependent CKD and kidney failure requiring dialysis. In pediatric CKD, the management of anemia aims not only to increase hemoglobin levels but also to minimize the need for blood transfusions, preserve functional capacity, and reduce the long-term treatment burden. Erythropoiesis-stimulating agents (ESAs) remain the cornerstone of anemia management in this population. A systematic review of ESA use in children with CKD reported that different ESA preparations and routes of administration were generally effective, although treatment should be individualized because pediatric evidence remains heterogeneous and higher ESA doses may be associated with harm [1]. Within this treatment landscape, recombinant human erythropoietin preparations usually require frequent administration, whereas darbepoetin alfa has a longer duration of action and permits extended dosing intervals. This pharmacologic difference is clinically relevant in children because each injection may add discomfort, caregiver burden, clinic contact, and potential adherence challenges. Darbepoetin alfa has been evaluated in several pediatric CKD populations, but the available evidence remains smaller than the adult literature. A prospective registry study of 319 children with CKD-related anemia receiving darbepoetin alfa for up to two years found that hemoglobin levels were generally maintained around the recommended range, with no new safety signals identified [2]. Earlier pediatric experience also supported darbepoetin alfa as an effective long-acting ESA. In an observational study of children aged 11 to 18 years with chronic renal failure, darbepoetin alfa was used at extended dosing intervals and achieved target hemoglobin in a substantial proportion of patients, including those switched from recombinant human erythropoietin [3]. Smaller reports in non-dialysis children and young infants similarly described hemoglobin correction with darbepoetin alfa and highlighted the practical interest in reducing painful injections and improving treatment acceptability [4,5]. These studies support darbepoetin alfa as a feasible pediatric ESA, but most were observational or small, and they were not primarily designed to quantify injection burden against recombinant erythropoietin beta. Dose requirement is also an important outcome in pediatric CKD anemia, because a higher ESA requirement may reflect reduced responsiveness, inflammation, dialysis adequacy, iron availability, or other comorbidity. In children receiving chronic peritoneal dialysis, a large international registry analysis showed that anemia control varied across regions and that ESA dose was inversely associated with survival, supporting the clinical relevance of ESA exposure as more than a dosing detail [6]. In pediatric maintenance hemodialysis, anemia targets remain difficult to achieve consistently. A recent dialysis-unit performance study reported that only a minority of children achieved quarterly hemoglobin targets despite ESA and iron management [7]. Another recent pediatric hemodialysis study found that erythropoietin resistance was associated with high C-reactive protein, low Kt/V, lower hemoglobin, and higher EPO dose, reinforcing that ESA requirement should be interpreted in relation to treatment response

and clinical context [8]. Adult randomized studies provide stronger indirect evidence that darbepoetin alfa can maintain hemoglobin with fewer injections than epoetin preparations. In dialysis patients, once-weekly darbepoetin alfa was non-inferior to thrice-weekly epoetin alfa in an Indian randomized phase III trial, and a Chinese randomized non-inferiority trial similarly supported once-weekly darbepoetin alfa compared with more frequent epoetin alfa dosing [9,10]. Economic findings remain less consistent. One randomized Canadian adult hemodialysis study found lower annual ESA cost with darbepoetin alfa than epoetin alfa, whereas a Saudi cost-effectiveness analysis favored epoetin beta over darbepoetin alfa in its local model [11,12]. These conflicting findings indicate that lower injection frequency may reduce administration-related burden, but it does not automatically prove lower total treatment cost. Targeted pediatric literature addressing dose requirement, injection burden, and cost implications of darbepoetin alfa versus recombinant erythropoietin beta remains limited, especially in South Asian children with CKD-related anemia. A recent systematic review and cost-effectiveness analysis comparing epoetin alfa and darbepoetin in children found limited and heterogeneous pediatric comparative evidence, with no clear hemoglobin advantage for either agent in pooled direct comparisons [13]. The present manuscript therefore evaluates monthly ESA dose requirement, injection frequency, hemoglobin response, and injection-related outcomes in children with CKD-related anemia treated with darbepoetin alfa or recombinant erythropoietin beta, with cost implications considered cautiously through observed treatment burden rather than formal economic evaluation.

METHODS & MATERIALS

This multicenter, open-label, randomized controlled study was conducted at the Department of Pediatric Nephrology, Bangladesh Institute of Child Health and Dhaka Shishu Children's Hospital, Dhaka, Bangladesh, and the Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The study duration was from October 2019 to September 2020. Children aged 1 to 18 years with CKD-related anemia were enrolled, including dialysis-independent CKD stages G3b to G5 and dialysis-dependent CKD G5d receiving maintenance hemodialysis. Eligible children had hemoglobin 8 to <11 g/dL, transferrin saturation >20%, serum ferritin >100 ng/mL for dialysis-independent CKD or >200 ng/mL for dialysis-dependent CKD, and adequate serum albumin. Children were excluded if they had severe anemia requiring blood transfusion, hemoglobin >11 g/dL at screening, GFR ≥60 mL/min/1.73 m², recent blood transfusion, active infection or inflammatory disease, hematologic or bleeding disorder, uncontrolled hypertension or hypertensive emergency, severe hyperparathyroidism, poor adherence to oral iron, prior ESA exposure within the restricted period, or refusal of consent. Participants were allocated to darbepoetin alfa or recombinant human erythropoietin beta. Darbepoetin alfa was administered subcutaneously at 0.75 µg/kg/week, with dosing every 2 weeks in dialysis-dependent children and once weekly in dialysis-independent children. Recombinant erythropoietin beta was administered subcutaneously at 100 IU/kg three times weekly in both dialysis-dependent and dialysis-independent children. Background management included nutritional support, oral iron, folic acid, and treatment of CKD-related biochemical abnormalities when clinically indicated. Hemoglobin was monitored during follow-up, and ESA dose adjustment was guided by hemoglobin concentration, rate of hemoglobin rise, current ESA dose, and clinical status. The intended hemoglobin target range was 11 to 12 g/dL, and dose holding or reduction was applied if hemoglobin rose excessively or exceeded the predefined safety threshold. The primary outcomes for the present analysis were monthly ESA dose requirement and monthly injection burden during the first evaluation period. Dose requirement was reported separately in drug-specific units, µg/month for darbepoetin alfa and IU/month for recombinant erythropoietin beta, because the two agents are not directly comparable by absolute dose unit. Injection burden was assessed by mean number of injections per month and grouped monthly injection-frequency categories. The absolute monthly injection reduction was calculated as the difference between mean monthly injections in the recombinant erythropoietin beta and darbepoetin alfa groups, and the relative injection reduction was calculated as the absolute reduction divided by the mean monthly injection frequency in the recombinant erythropoietin beta group. Secondary outcomes included hemoglobin response at 16 weeks in the intention-to-treat cohort, hemoglobin response at 48 weeks in the per-protocol cohort, injection-site pain, and hypertension. Continuous variables were summarized as mean ± standard deviation, and categorical variables were summarized as frequency and percentage. Between-group comparisons of continuous variables were performed using unpaired t tests, and within-group hemoglobin changes were assessed using paired t tests where applicable. Safety outcomes were summarized descriptively using frequency and percentage. Analyses were performed using SPSS version 23.0, and $p < .05$ was considered statistically significant. The study protocol was approved by the Ethical Review Committee of Bangladesh Institute of Child Health, Dhaka. Written informed consent was obtained from parents or legal guardians before enrollment, and participant confidentiality was maintained throughout data collection, analysis, and reporting.

RESULTS

A total of 44 children were included in the 16-week intention-to-treat analysis, with 19 children allocated to darbepoetin alfa and 25 allocated to recombinant human erythropoietin beta. The 48-week per-protocol analysis included 33 children, with 15 children in the darbepoetin alfa group and 18 in the rHuEPO beta group. The analysis focused on ESA dose requirement, monthly injection frequency, hemoglobin response, injection-related adverse events, and cost implications based on observed treatment burden. The overall cohort included 44 children, with 19/44 (43.2%) in the darbepoetin alfa group and 25/44 (56.8%) in the rHuEPO beta group. The largest age category was >5 to 10 years, 26/44 (59.1%). Female children accounted for 26/44 (59.1%) of the cohort. Moderate anemia was present in 30/44 (68.2%) children, including 16/19 (84.2%) in the darbepoetin alfa group and 14/25 (56.0%) in the rHuEPO beta group (*Table I*).

Table I
Baseline demographic and clinical characteristics of children receiving ESA therapy.

Characteristic	Overall cohort, n = 44	Darbepoetin alfa, n = 19	rHuEPO beta, n = 25
Age			
Age 1 to 5 years	12 (27.3)	2 (10.5)	5 (20.0)
Age >5 to 10 years	26 (59.1)	15 (78.9)	10 (40.0)
Age >10 to 15 years	6 (13.6)	2 (10.5)	10 (40.0)
Sex			
Male	18 (40.9)	5 (26.3)	13 (52.0)
Female	26 (59.1)	14 (73.7)	12 (48.0)
Residence			
Rural	12 (27.3)	6 (31.6)	6 (24.0)
Urban	32 (72.7)	13 (68.4)	19 (76.0)
Baseline anemia category			
Moderate anemia, Hb >8 to 10 g/dL	30 (68.2)	16 (84.2)	14 (56.0)
Mild anemia, Hb >10 to <11 g/dL	14 (31.8)	3 (15.8)	11 (44.0)

Note. Values are n (%) unless otherwise indicated. ESA = erythropoiesis-stimulating agent; Hb = hemoglobin; rHuEPO = recombinant human erythropoietin beta.

Dialysis-independent CKD was present in 26/44 (59.1%) children, including 12/19 (63.2%) in the darbepoetin alfa group and 14/25 (56.0%) in the rHuEPO beta group. Maintenance hemodialysis was present in 18/44 (40.9%) children, including 7/19 (36.8%) and 11/25 (44.0%), respectively. Mean body weight differed by 2.0 kg between groups, 23.0 ± 6.54 kg versus 25.0 ± 6.54 kg, p = .084 (*Table II*).

Table II
CKD stage, dialysis status, and body weight at baseline.

Characteristic	Overall cohort, n = 44	Darbepoetin alfa, n = 19	rHuEPO beta, n = 25
CKD stage			
CKD G3b	6 (13.6)	2 (10.5)	4 (16.0)
CKD G4	16 (36.4)	8 (42.1)	8 (32.0)
CKD G5, dialysis-independent	4 (9.1)	2 (10.5)	2 (8.0)
CKD G5d, dialysis-dependent	18 (40.9)	7 (36.8)	11 (44.0)
Dialysis status			
Dialysis-independent CKD	26 (59.1)	12 (63.2)	14 (56.0)
Maintenance hemodialysis	18 (40.9)	7 (36.8)	11 (44.0)

Note. Values are n (%) or M ± SD. CKD = chronic kidney disease; rHuEPO = recombinant human erythropoietin beta.

The mean monthly darbepoetin alfa dose remained 60 µg/month during both the titration period and the first evaluation period. The mean monthly rHuEPO beta dose increased from 24,000.5 IU/month to 30,000 IU/month, an absolute increase of 5,999.5 IU/month and a relative increase of approximately 25.0%. The protocol schedule required less frequent administration for darbepoetin alfa than for rHuEPO beta (*Table III*).

Table III
ESA regimen and monthly dose requirement.

Characteristic	Darbepoetin alfa, n = 19	rHuEPO beta, n = 25
Protocol regimen		
Route of administration	Subcutaneous	Subcutaneous
Protocol dose	0.75 µg/kg/week	100 IU/kg three times weekly
Dosing in dialysis-dependent patients	Every 2 weeks	Three times weekly
Dosing in dialysis-independent patients	Once weekly	Three times weekly
Mean monthly ESA dose		
Titration period dose	60 ± 0.43 µg/month	24,000.5 ± 0.63 IU/month
First evaluation period dose	60 ± 0.63 µg/month	30,000 ± 0.99 IU/month
Absolute dose change from titration to first evaluation	0 µg/month	+5,999.5 IU/month
Relative dose change from titration to first evaluation	0.0%	+25.0%

Note. Values are M ± SD where applicable. ESA = erythropoiesis-stimulating agent; rHuEPO = recombinant human erythropoietin beta.

Mean monthly injection frequency was 4.5 ± 0.23 with darbepoetin alfa and 10.2 ± 0.33 with rHuEPO beta. Darbepoetin alfa required 5.7 fewer injections per month, corresponding to a 55.9% lower injection frequency than rHuEPO beta. rHuEPO beta required approximately 2.27 times as many monthly injections. In the darbepoetin alfa group, 18/19 (94.7%) children were in the lowest injection-frequency category, compared with 8/25 (32.0%) in the rHuEPO beta group (*Table IV*).

Table IV
Monthly injection burden during the first evaluation period.

Monthly injection frequency	Darbepoetin alfa, n = 19	rHuEPO beta, n = 25
Injection frequency category		
1 to <4 injections/month	18 (94.7)	8 (32.0)
5 to 8 injections/month	1 (5.3)	6 (24.0)
9 to 12 injections/month	0 (0.0)	9 (36.0)
13 to 16 injections/month	0 (0.0)	2 (8.0)
Mean monthly injections		
Monthly injections, M ± SD	4.5 ± 0.23	10.2 ± 0.33
Absolute reduction with darbepoetin alfa	5.7 fewer injections/month	Reference
Relative reduction with darbepoetin alfa	55.9% fewer injections/month	Reference
rHuEPO beta injection ratio	Reference	2.27 times darbepoetin alfa

Note. Values are n (%) or M ± SD. Relative reduction was calculated as: (10.2 − 4.5) / 10.2 × 100.

At 16 weeks, mean hemoglobin was 10.53 ± 0.88 g/dL in the darbepoetin alfa group and 10.53 ± 0.63 g/dL in the rHuEPO beta group, p = .968. Mean hemoglobin increase at 16 weeks was 2.02 ± 1.06 g/dL versus 1.73 ± 1.29 g/dL, with a between-group difference of 0.29 g/dL, p = .429. At 48 weeks, hemoglobin was 11.19 ± 0.67 g/dL versus 10.75 ± 0.63 g/dL, with a between-group difference of 0.44 g/dL, p = .037. The 48-week hemoglobin increase was 2.73 ± 0.78 g/dL versus 1.83 ± 0.83 g/dL, with a difference of 0.90 g/dL, p = .004 (*Table V*).

Table V
Hemoglobin response as efficacy context for dose and injection burden.

Characteristic	Darbepoetin alfa n = 19	rHuEPO beta n = 25	Difference	p
ITT analysis, 16-week evaluation				
Baseline hemoglobin, g/dL	8.55 ± 0.60	8.83 ± 1.23	0.28	.490
Hemoglobin at 16 weeks, g/dL	10.53 ± 0.88	10.53 ± 0.63	0.00	.968
Change from baseline, g/dL	2.02 ± 1.06	1.73 ± 1.29	0.29	.429
PP analysis, 48-week evaluation				
----------	n = 15	n = 18	-	-
Baseline hemoglobin, g/dL	8.55 ± 0.60	8.83 ± 0.70	0.28	.490
Hemoglobin at 48 weeks, g/dL	11.19 ± 0.67	10.75 ± 0.63	0.44	.037
Change from baseline, g/dL	2.73 ± 0.78	1.83 ± 0.83	0.90	.004

Note. Values are M ± SD. ITT = intention-to-treat; PP = per-protocol; rHuEPO = recombinant human erythropoietin beta.

Injection-site pain was reported in 18/19 (94.7%) children receiving darbepoetin alfa and 10/25 (40.0%) receiving rHuEPO beta. Hypertension was reported in 7/19 (36.8%) and 9/25 (36.0%), respectively. The absolute difference in injection-site pain was 54.7 percentage points, while the absolute difference in hypertension was 0.8 percentage points (*Table VI*).

Table VI
Injection-related and safety outcomes in the ITT cohort.

Adverse event	Darbepoetin alfa, n = 19	rHuEPO beta, n = 25
Injection-site pain	18 (94.7)	10 (40.0)
Hypertension	7 (36.8)	9 (36.0)

Note. Values are n (%). Percentages were calculated using ITT group denominators. These safety outcomes are presented descriptively.

DISCUSSION

The present study evaluated dose requirement, injection burden, hemoglobin response, and injection-related outcomes in children with CKD-related anemia treated with darbepoetin alfa or recombinant erythropoietin beta. The main practical finding was that darbepoetin alfa required substantially fewer monthly injections than rHuEPO beta. Mean monthly injection frequency was 4.5 ± 0.23 injections/month with darbepoetin alfa and 10.2 ± 0.33 injections/month with rHuEPO beta, corresponding to 5.7 fewer injections/month and a 55.9% relative reduction. This difference is clinically relevant in pediatric CKD, where repeated injections add discomfort, caregiver involvement, clinic contact, and potential treatment fatigue. The reduced injection burden observed with darbepoetin alfa is consistent with the pharmacologic rationale for long-acting ESA therapy. In pediatric CKD literature, conventional recombinant erythropoietin has generally been described as requiring two to three injections per week, whereas darbepoetin alfa has been used at longer dosing intervals because of its prolonged half-life and reduced clearance [3,5]. In adult dialysis trials, once-weekly darbepoetin alfa was shown to maintain hemoglobin response comparable to more frequent epoetin alfa administration [9,10]. Although these adult findings cannot be directly transferred to children, they support the observed direction of effect in the present cohort. The quantified monthly injection difference in this study, 4.5 versus 10.2 injections/month, adds practical pediatric data to an area where direct comparative reporting remains limited. Dose requirement also differed between the two treatment groups. The mean monthly darbepoetin alfa dose remained stable at 60 µg/month during both the titration and first evaluation periods, while the mean monthly rHuEPO beta dose increased from 24,000.5 IU/month to 30,000 IU/month, representing an approximate 25.0% increase. These values should not be interpreted as directly comparable absolute doses because darbepoetin alfa and rHuEPO beta are measured in different units. However, the pattern suggests that darbepoetin alfa was maintained without dose escalation during the early treatment period, whereas rHuEPO beta required a higher monthly dose by the first evaluation period. This finding is compatible with pediatric registry experience, where darbepoetin alfa was

used over time to maintain hemoglobin levels in children with CKD-related anemia [2]. It also reinforces the importance of reporting ESA exposure as an outcome, because higher ESA requirement may reflect reduced responsiveness, inflammation, dialysis adequacy, or iron availability. In pediatric dialysis cohorts, ESA resistance has been linked with higher EPO dose, lower hemoglobin, inflammatory markers, and dialysis adequacy [6,8]. Hemoglobin response provides important context for interpreting the lower injection burden. At 16 weeks, mean hemoglobin was identical in the two groups, 10.53 ± 0.88 g/dL with darbepoetin alfa and 10.53 ± 0.63 g/dL with rHuEPO beta, p = .968. The mean increase from baseline was also not significantly different, 2.02 ± 1.06 g/dL versus 1.73 ± 1.29 g/dL, p = .429. This indicates that the lower injection frequency with darbepoetin alfa was not associated with inferior short-term hemoglobin response. Similar comparative findings were reported in the recent pediatric systematic review and meta-analysis, where no clear hemoglobin advantage was shown for darbepoetin alfa over recombinant erythropoietin in pooled direct comparisons [13]. The broader pediatric ESA literature also supports that different ESA preparations can be effective, although the evidence base remains heterogeneous [1]. At 48 weeks, a more favorable hemoglobin response was observed in the darbepoetin alfa per-protocol cohort. Mean hemoglobin was 11.19 ± 0.67 g/dL with darbepoetin alfa and 10.75 ± 0.63 g/dL with rHuEPO beta, p = .037. The mean hemoglobin increase from baseline was also greater with darbepoetin alfa, 2.73 ± 0.78 g/dL versus 1.83 ± 0.83 g/dL, p = .004. This finding is clinically meaningful because the darbepoetin alfa group reached the target range while maintaining a lower injection frequency. Pediatric darbepoetin alfa studies have reported hemoglobin values around 11 g/dL during follow-up, supporting the plausibility of this response [2,3]. However, the 48-week finding should be interpreted cautiously because it was based on a smaller per-protocol cohort of 33 children, and attrition may have influenced the observed treatment difference. Injection-site pain was an important counterbalancing finding. Pain was reported in 18/19 children receiving darbepoetin alfa and 10/25 receiving rHuEPO beta, corresponding to 94.7% versus 40.0%. Therefore, darbepoetin alfa reduced the number of injections but did not reduce reported injection discomfort in this cohort. Pediatric literature has recognized painful injections as a practical barrier to ESA acceptability and adherence [4,5]. The present finding suggests that injection burden should be considered in two dimensions: frequency and tolerability. A less frequent injection schedule may still be burdensome if each injection is more painful. This distinction is important for counseling families and for selecting ESA regimens in children who require long-term therapy. Hypertension was similar between groups, occurring in 36.8% of children receiving darbepoetin alfa and 36.0% receiving rHuEPO beta. Given the high baseline burden of hypertension in pediatric CKD, these descriptive findings should not be interpreted as treatment-attributable differences. Larger pediatric safety data have not identified new safety signals with darbepoetin alfa, although adverse events remain common in children with advanced CKD [2]. In the present study, the main safety distinction was injection-site pain rather than hypertension. The cost implications of these findings should be framed carefully. Direct costs were not measured, and no formal cost-effectiveness analysis was performed. The observed reduction of 5.7 injections/month with darbepoetin alfa may reduce administration contacts, caregiver time, and visit-related burden when injections require facility attendance. However, total treatment cost depends on drug acquisition price, vial size, wastage, administration charges, transport cost, caregiver indirect cost, and health-system reimbursement. Cost studies have shown mixed results: lower annual ESA cost with darbepoetin alfa was reported in one adult Canadian randomized study, whereas epoetin beta was favored in a Saudi cost-effectiveness model [11,12]. Pediatric modeling has also suggested that rHuEPO may be more cost-effective as initial therapy in some contexts [13]. Therefore, this study supports lower injection-related burden with darbepoetin alfa, but not lower total cost.

LIMITATIONS

The study has several limitations. The sample size was small, and the 48-week analysis was limited to the per-protocol cohort. Dose and injection burden were reported using available treatment-period summaries rather than detailed patient-level dose trajectories. Injection-site pain was recorded descriptively, without a standardized pain scale. Direct economic data were not collected, so cost implications remain inferential. Despite these limitations, the findings provide clinically relevant pediatric data from a South Asian CKD cohort and support darbepoetin alfa as a lower-frequency ESA option with maintained hemoglobin response, while emphasizing that reduced injection frequency must be weighed against injection-site pain and local cost conditions.

CONCLUSION

Darbepoetin alfa was associated with a substantially lower injection burden than recombinant erythropoietin beta while maintaining comparable short-term hemoglobin response in children with CKD-related anemia. Sustained treatment was accompanied by favorable long-term hemoglobin outcomes, although injection-site pain was reported more frequently with darbepoetin alfa, whereas hypertension occurred at similar frequencies in both groups. These findings suggest that darbepoetin alfa may offer a practical advantage by reducing treatment burden through less frequent administration, while maintaining therapeutic efficacy. Further multicenter studies with larger pediatric populations and formal pharmacoeconomic evaluation are warranted to confirm these findings and clarify their implications for routine clinical practice.

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CONFLICT OF INTEREST

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ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

REFERENCES

1. Bruce G, Schulga P, Reynolds BC. Use of erythropoiesis-stimulating agents in children with chronic kidney disease: a systematic review. Clin Kidney J. 2022 Feb 26;15(8):1483–505. doi:10.1093/ckj/sfac058 PubMed PMID: 35892014; PubMed Central PMCID: PMC9308099.
2. Schaefer F, Hoppe B, Jungraithmayr T, Klaus G, Pape L, Farouk M, et al. Safety and usage of darbepoetin alfa in children with chronic kidney disease: prospective registry study. Pediatr Nephrol. 2016;31:443–53. doi:10.1007/s00467-015-3225-0 PubMed PMID: 26482252; PubMed Central PMCID: PMC4756039.
3. André JL, Deschênes G, Boudailliez B, Broux F, Fischbach M, Gagnadoux MF, et al. Darbepoetin, effective treatment of anaemia in paediatric patients with chronic renal failure. Pediatr Nephrol. 2007 May 1;22(5):708–14. doi:10.1007/s00467-006-0402-1
4. Gaydarova M, Boueva A, Marinova S, Zlatanova G. USE OF DARBEPOETIN ALFA (ARANESP®) FOR ANEMIA TREATMENT IN CHILDREN WITH CHRONIC KIDNEY DISEASE – CLINICAL EXPERIENCE OF BULGARIAN PEDIATRIC GROUP. J of IMAB. 2017 Jan 17;23(1):1421–6. doi:10.5272/jimab.2017231.1421
5. Libudzic-Nowak AM, Cachat F, Pascual M, Chehade H. Darbepoetin alfa in young infants with renal failure: single center experience, a case series and review of the literature. Frontiers in pediatrics. 2018;6:398.
6. Borzych-Duzalka D, Bilginer Y, Ha IS, Bak M, Rees L, Cano F, et al. Management of anemia in children receiving chronic peritoneal dialysis. Journal of the American Society of Nephrology. 2013;24(4):665–76.
7. Khalil MA, Kasem MF, El-Hakim IZ, Abd Elhafez AM, El Farsy MS, Said RM. Key

performance indicators for monitoring of anemia management and iron status in children attending a pediatric dialysis unit: the experience of Ain Shams University. J Nephrol. 2024 Sep 1;37(7):1967–72. doi:10.1007/s40620-024-02017-3
8. Helmy R, Fadel FI, Galal RE, Mohammed AM, Sayed S. Erythropoietin resistance among pediatric patients on chronic hemodialysis: A cross-sectional study. Pediatr Nephrol. 2025 Dec 1;40(12):3725–32. doi:10.1007/s00467-025-06776-4
9. Sinha SD, Bandi VK, Bheemareddy BR, Thakur P, Chary S, Mehta K, et al. Efficacy, tolerability and safety of darbepoetin alfa injection for the treatment of anemia associated with chronic kidney disease (CKD) undergoing dialysis: a randomized, phase-III trial. BMC Nephrol. 2019 Mar 13;20(1):90. doi:10.1186/s12882-019-1209-1
10. Chen N, Xing C, Niu J, Liu B, Fu J, Zhao J, et al. Darbepoetin alfa injection versus epoetin alfa injection for treating anemia of Chinese hemodialysis patients with chronic kidney failure: A randomized, open-label, parallel-group, non-inferiority Phase III trail. Chronic Diseases and Translational Medicine. 2022;8(1):59–70. doi:10.1002/cdt3.13
11. Woodland AL, Murphy SW, Curtis BM, Barrett BJ. Costs Associated With Intravenous Darbepoetin Versus Epoetin Therapy in Hemodialysis Patients: A Randomized Controlled Trial. Can J Kidney Health Dis. 2017 Jan 1;4:2054358117716461. doi:10.1177/2054358117716461
12. AlKharboush H, Alshehri F, Alatwi I, Al Karni K, Alatawi A, Hamdan AM. The Cost-Effectiveness of Using Epoetin-Beta Versus Darbepoetin-Alfa for the Treatment of Anemia Among Chronic Hemodialysis Patients. Cureus. 12(12):e11895. doi:10.7759/cureus.11895 PubMed PMID: 33415047; PubMed Central PMCID: PMC7781860.
13. Bertazza Partigiani N, D'Uva A, Vigezzi S, Brazzale AR, Vidal E. Comparative efficacy of epoetin alfa vs. darbepoetin in children with chronic kidney disease: a systematic review, meta-analysis and cost-effectiveness analysis. J Nephrol. 2025 Nov;38(8):2095–109. doi:10.1007/s40620-025-02303-8 PubMed PMID: 40349276; PubMed Central PMCID: PMC12630148.