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Original Article

Darbepoetin alfa is more effective than epoetin-β in suppressing hepcidin and improving iron utilization in maintenance hemodialysis patients

Jinfeng Tan[1], Huimin Yan[1], Xin Li[1], Yong Chen[2]

[1]Department of Pharmacy, Suzhou BenQ Medical Center, Suzhou 215000, Jiangsu Province, China; [2]Department of Pharmacy, Nanjing BenQ Medical Center, The Affiliated BenQ Hospital of Nanjing Medical University, Nanjing 210019, Jiangsu Province, China

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Abstract: Objective: This study aimed to compare the dynamics of serum hepcidin and iron metabolism markers in maintenance hemodialysis patients treated with reconstituted human Erythropoietin-β (EPO-β) and darbepoetin alfa (DA). Methods: This retrospective observational study included 105 patients on maintenance hemodialysis. Of these, 64 were in the EPO-β group (administered 2-3 times weekly) and 41 in the DA group (administered once every two weeks). Serum hepcidin, ferritin, transferrin saturation (TSAT), high-sensitivity C-reactive protein (hs-CRP), serum iron and hemoglobin (Hb) were measured at baseline, at week 8 and at week 12. A correlation analysis was performed. For the repeated measures analysis of variance comparing multiple time points (baseline, week 8 and week 12) between the two groups, Bonferroni post-hoc tests were used to perform pairwise comparisons. Results: Serum hepcidin decreased continuously in both groups during the 12-week treatment duration. At week 12, the DA group exhibited significantly lower hepcidin levels compared with EPO-β group. The Δhepcidin from baseline to week 12 was significantly greater in the DA group. The DA group also showed significant improvements in iron metabolism markers, with a greater decrease in TSAT, and a greater increase in serum iron compared to the EPO-β group. The erythropoiesis-stimulating agents resistance index (ERI) was significantly lower in the DA group than in the EPO-β group. LnΔhepcidin showed a positive correlation with LnΔFerritin, LnΔTSAT, LnΔSerum iron, and LnΔHb. The rates of adverse events were comparable between the two groups. Conclusion: Compared to EPO-β, DA more effectively suppresses hepcidin, improves iron metabolism markers, and achieves higher erythropoietic efficiency, with comparable Hb response rates and safety profiles between the two groups.

Keywords: Erythropoietin, darbepoetin alfa, hepcidin, iron metabolism, hemodialysis

Introduction

Renal anemia is defined as anemia resulting from absolute or relative insufficiency of erythropoietin (EPO) production due to various kidney diseases, combined with the detrimental effects of uremic toxins on erythropoiesis and red blood cell survival [1, 2]. Renal anemia impairs patients' quality of life and is associated with an increased risk of cardiovascular events and mortality [3, 4]. The global burden of anemia attributable to chronic kidney disease has increased substantially over recent decades, highlighting the urgent need for optimized therapeutic strategies [5]. Erythropoiesis-stimulating agents (ESAs) have been the standard treatment for renal anemia for decades, with currently available options including recombinant human EPO (rHuEPO), darbepoetin alfa (DA), and continuous erythropoietin receptor activator (CERA). All three types of ESAs significantly reduce transfusion requirements and alleviate anemia-related symptoms in patients with chronic kidney disease (CKD) [6, 7]. Currently, there is no conclusive evidence to demonstrate differences among these three types of ESAs with regard to hemoglobin (Hb) elevation, adverse event profiles, or improvement in quality of life [8, 9].

Hepcidin, a 25-amino acid peptide hormone produced primarily by hepatocytes, is the master regulator of systemic iron homeostasis and plays a critical role in the pathogenesis of renal

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anemia. It controls iron absorption and recycling by binding to ferroportin and induces its degradation [10]. In maintenance hemodialysis patients, hepcidin levels are often elevated and are positively correlated with inflammatory markers (IL-6, hs-CRP) and iron parameters (ferritin, TSAT) [11, 12]. Another study shows that serum hepcidin-25 levels were significantly negatively correlated with the erythropoiesis-stimulating agents resistance index (ERI) in Japanese patients receiving hemodialysis. The results suggest that hepcidin-25 levels might be associated with ERI and the administration of oral iron-containing preparations [11]. Many studies have shown that hepcidin level is positively correlated with the degree of anemia and inflammation, and the increase of hepcidin seriously affects the prognosis of chronic renal failure [13-15].

Recent studies have shown that different ESAs exhibit different patterns of action on hepcidin. According to Takazawa et al., short-acting EPOs temporarily increase hepcidin levels before they rapidly return to baseline. Long-acting ESAs, on the other hand, exhibit a biphasic response, with levels tending to decline again 5 to 7 days after administration [16]. The most recent network meta-analysis highlights the importance of iron metabolism management in the treatment of renal anemia and shows that optimal selection of ESAs significantly affects iron utilization efficiency [17]. The relationship between hepcidin and ESAs is also the subject of research. Hepcidin is also discussed as a potential biomarker to predict therapy success, but its clinical utility remains under discussion [18, 19].

Given that the comparative effects of different ESA types on hepcidin dynamics remain incompletely understood. This study aimed to compare the dynamic changes in serum hepcidin and iron metabolism markers in maintenance hemodialysis patients treated with EPO-β versus DA over a 12-week treatment period.

Materials and methods

Study design and participants

This was a single-center, retrospective observational study conducted at the Suzhou BenQ Medical Center from May 2023 to May 2025 that collected maintenance hemodialysis patients. The study protocol was approved by the Institutional Ethics Committee of Suzhou BenQ Medical Center, and informed consent was waived due to the retrospective nature of the study.

Inclusion criteria were: (1) age ≥ 18 years; (2) diagnosis of end-stage renal disease (uremia) with maintenance hemodialysis ≥ 6 months; (3) continuous treatment with a single ESA during the 12-week observation period; (4) at least three serum samples for hepcidin and iron metabolism measurements (at weeks 0, 8, and 12); and (5) complete clinical records.

Exclusion criteria were: (1) acute infection, major trauma, active bleeding, or major surgery during the observation period; (2) blood transfusion or use of other ESAs during the observation period; (3) active malignancy, severe liver disease, or uncontrolled inflammatory disease.

Data collection

A total of 105 maintenance hemodialysis patients were included, comprising 64 patients in the EPO-β group (epoetin beta, 0.3 mL: 5,000 IU, Shanghai Roche Pharmaceuticals Co., Ltd., administered 2-3 times weekly) and 41 patients in the DA group (DA, 40 μg, Kyowa Kirin (China) Pharmaceutical Co., Ltd., administered once every 2 weeks or monthly).

Baseline data included demographic characteristics, dialysis vintage, dialysis adequacy (Kt/V), and laboratory parameters including Hb, serum hepcidin-25, serum iron, ferritin, transferrin saturation (TSAT), total iron-binding capacity (TIBC), high-sensitivity C-reactive protein (hs-CRP), albumin, serum creatinine, and intact parathyroid hormone (iPTH).

Outcomes

The primary outcome was the change in hepcidin from baseline to week 12. Secondary outcomes included Hb response rate, the percentage change in hepcidin, ERI, ESA dosing, changes in Hb, serum iron, ferritin, TSAT, and hs-CRP from baseline to week 12, and adverse events (AEs).

Dynamic data were collected at weeks 0 (baseline), 8, and 12 (± 7 days), including serum hepcidin, Hb, serum iron, ferritin, TSAT, and hs-CRP. ESA dosing records were also extracted.

AEs were collected and defined according to the internationally recognized standards established by the International Council for Harmonisation (ICH) and the Good Clinical Practice (GCP) guidelines [20].

Specifically, for each patient, the percentage change in hepcidin was calculated as [(hepcidin at week 12 - hepcidin at baseline)/hepcidin at baseline] × 100%. Hb response rate (≥ 11 g/dL) was defined as the proportion of patients achieving a Hb level ≥ 11 g/dL after 12 weeks of treatment. ERI is a validated measure of responsiveness to ESAs, calculated as the weekly ESA dose per kilogram of body weight divided by the Hb level using the formula: ERI = Weekly ESA dose (IU/kg)/Hb (g/dL). One μg of darbepoetin alfa is approximately equivalent to 200 IU of epoetin alfa. The reported Δhepcidin, Δferritin, ΔTSAT, ΔSerum iron and LnΔHb values represent the arithmetic mean of these individual changes.

Statistical analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables with a normal distribution were shown as mean ± standard deviation (SD) and were compared using independent-samples t-tests. Non-normally distributed variables were shown as median (interquartile range, IQR) and were compared using Mann-Whitney U tests. Categorical variables were shown as n (%) and were compared using chi-square tests. Repeated measures analysis of variance (ANOVA) was used to compare the changes in hepcidin and iron metabolism markers between the two groups over time. Correlation analyses were done using Pearson's correlation coefficient for normally distributed variables and Spearman's rank correlation coefficient for non-normally distributed variables. The natural logarithmic transformation (Ln) was applied because the Δhepcidin, Δferritin, ΔTSAT, Δserum iron, and ΔHb values were not normally distributed, as confirmed by the Shapiro-Wilk test ($P < 0.05$). Logarithmic transformation is a standard approach to normalize skewed data before performing parametric correlation analysis. The correlation between Ln-transformed variables reflects the relationship between the relative (percentage) changes of the original variables. For example, a positive correlation between LnΔhepcidin and LnΔFerritin indicates that a greater relative decrease in hepcidin is associated with a greater relative decrease in ferritin. A two-sided *P*-value < 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 105 patients were included, among whom, 41 patients received DA treatment. Baseline characteristics, including demographic characteristics, dialysis vintage, Kt/V, and Hb, serum hepcidin-25, serum iron, ferritin, TSAT, TIBC, hs-CRP, albumin, serum creatinine, and iPTH were comparable between the two groups (all $P > 0.05$) (**Table 1**).

Dynamic changes in hepcidin levels

At baseline and week 8, there was no significant difference in serum hepcidin levels between the two groups (both $P > 0.05$). However, at week 12, the DA group exhibited significantly lower hepcidin levels compared with EPO-β group ($P = 0.010$). The Δhepcidin from baseline to week 12 was significantly greater in the DA group ($P < 0.001$), corresponding to a 51.64% reduction in hepcidin levels, compared with a 35.75% reduction in the EPO-β group ($P < 0.001$) (**Table 2**).

Dynamic changes in iron metabolism markers

At baseline and week 8, there were no significant differences in the values of the three iron metabolism markers between the two groups (all $P > 0.05$). At week 12, the ferritin values in the DA group were significantly lower than in the EPO-β group ($P = 0.024$), while the TSAT in the EPO-β group was significantly higher ($P < 0.001$). Comparing the TSAT change from baseline to week 12, the DA group showed a significantly greater decline ($P < 0.001$). Although there was no significant difference in serum iron levels between the two groups at week 12, the increase from baseline in the DA group was significantly greater ($P < 0.001$). The change in ferritin did not differ significantly between the two groups ($P = 0.576$) (**Table 3**).

Dynamic changes in Hb

Both groups showed similar increasing trends in Hb levels over the 12-week treatment period.

Table 1. Baseline characteristics of study patients

Characteristic	EPO-β group (n = 64)	DA group (n = 41)	*P* value
Age (years)	58.36 ± 11.64	56.63 ± 14.10	0.497
Male, n (%)	39 (60.9)	28 (68.3)	0.438
BMI (kg/m^2)	23.38 ± 3.09	24.35 ± 3.55	0.144
Dialysis vintage (months)	34.00 (21.25-55.75)	27.0 (18.0-56.5)	0.435
Kt/V	1.412 ± 0.240	1.370 ± 0.334	0.455
Hb (g/dL)	9.391 ± 0.792	9.441 ± 0.746	0.747
Hepcidin (ng/mL)	73.25 (56.23-93.63)	86.70 (58.45-118.20)	0.302
Serum iron (μmol/L)	11.410 ± 3.484	9.951 ± 4.231	0.570
Ferritin (ng/mL)	368.0 (263.0-502.8)	320.0 (225.5-531.5)	0.338
TSAT (%)	29.90 (24.75-32.48)	27.90 (22.20-31.15)	0.069
TIBC (μmol/L)	47.530 ± 9.390	46.820 ± 7.740	0.685
hs-CRP (mg/L)	4.650 (2.950-7.050)	5.400 (3.350-8.700)	0.265
Albumin (g/L)	39.560 ± 3.882	38.380 ± 3.605	0.122
Creatinine (μmol/L)	922.1 ± 189.5	886.9 ± 189.2	0.355
iPTH (pg/mL)	265.0 (169.0-350.8)	244.0 (153.3-373.5)	0.879

BMI: body mass index; Hb: hemoglobin; Kt/V: dialysis adequacy; TSAT: transferrin saturation; TIBC: total iron-binding capacity; hs-CRP: high-sensitivity C-reactive protein; iPTH: intact parathyroid hormone; EPO-β: Erythropoietin-β; DA: darbepoetin alfa.

Table 2. Dynamic changes in serum hepcidin levels

Time point	EPO-β group	DA group	*P* value
Baseline (ng/mL)	73.25 (56.23-93.63)	86.70 (58.45-118.20)	0.302
Week 8 (ng/mL)	53.30 (46.63-75.68)	59.05 (38.88-86.75)	0.938
Week 12 (ng/mL)	49.60 (33.98-61.33)	38.55 (26.53-52.50)	0.010**
Δhepcidin (ng/mL)	-30.11 ± 18.42	-45.45 ± 22.67	< 0.001***
Δhepcidin (%)	-35.75 ± 6.56	-51.64 ± 5.92	< 0.001***

**P < 0.01, ***P < 0.001 compared between the two groups. EPO-β: Erythropoietin-β; DA: darbepoetin alfa.

Table 3. Dynamic changes in iron metabolism markers

Parameter	Group	Baseline	Week 8	Week 12	Δ value
Ferritin (ng/mL)	EPO-β group	368.0 (263.0-502.8)	354.0 (257.0-503.3)	352.5 (222.0-470.0)	-53.00 (-69.25-36.00)
	DA group	320.0 (225.5-531.5)	301.0 (205.5-478.5)	302.5 (178.0-417.3)	-75.50 (-231.8-54.50)
P		0.338	0.223	0.025*	0.576
TSAT (%)	EPO-β group	29.90 (24.75-32.48)	31.35 (27.18-34.08)	33.15 (27.60-36.63)	3.074 ± 1.058
	DA group	27.90 (22.20-31.15)	31.25 (25.60-35.85)	16.15 (11.95-21.43)	-9.614 ± 8.727
P		0.069	0.717	< 0.001***	< 0.001***
Serum iron (μmol/L)	EPO-β group	11.410 ± 3.484	12.890 ± 3.897	13.640 ± 3.975	2.159 ± 0.776
	DA group	9.951 ± 4.231	13.110 ± 4.698	13.350 ± 5.082	3.846 ± 1.288
P		0.570	0.803	0.458	< 0.001***

*P < 0.05, ***P < 0.001 compared between the two groups. EPO-β: Erythropoietin-β; DA: darbepoetin alfa; TSAT: transferrin saturation.

However, there was no significant difference in Hb levels between the two groups at baseline, week 8 and week 12 (all P > 0.05). Similarly, the ΔHb was comparable between the two groups (P = 0.614) (**Table 4**).

Correlation analysis

Significant correlations were observed between hepcidin changes and changes in iron metabolism markers. LnΔhepcidin showed a posi-

Table 4. Dynamic changes in Hb levels

Time point	EPO-β group	DA group	*P* value
Baseline (g/dL)	9.391 ± 0.792	9.441 ± 0.746	0.747
Week 8 (g/dL)	10.820 ± 0.978	10.720 ± 0.863	0.447
Week 12 (g/dL)	11.170 ± 1.019	11.330 ± 0.920	0.931
ΔHb (g/dL)	1.781 ± 0.311	1.795 ± 1.143	0.614

EPO-β: Erythropoietin-β; DA: darbepoetin alfa; Hb: hemoglobin.

Table 5. Correlation analysis of hepcidin changes with iron metabolism markers

Variable	Correlation coefficient (r)	*P* value
LnΔFerritin	0.285	0.009
LnΔTSAT	0.234	0.036
LnΔSerum iron	0.307	0.005
LnΔHb	0.250	0.020

TSAT: transferrin saturation; EPO-β: Erythropoietin-β; DA: darbepoetin alfa.

tive correlation with LnΔFerritin, LnΔTSAT, LnΔSerum iron and LnΔHb (**Table 5**).

Hb response and erythropoietin resistance

At week 12, the proportion of patients achieving Hb ≥ 11 g/dL was comparable between the two groups (P = 0.534). However, the ERI was significantly lower in the DA group (P < 0.001), indicating higher erythropoietic efficiency (**Table 6**).

Safety evaluation

The rates of adverse events were comparable between the two groups (P > 0.05), with no severe adverse events reported in either group. The most common adverse events were hypertension, arteriovenous fistula thrombosis, and injection site reactions (**Table 7**).

Discussion

This study compared the dynamic changes in hepcidin and iron metabolism markers in maintenance hemodialysis patients treated with EPO-β versus DA. The results showed that DA was superior to EPO-β in inhibiting hepcidin, improving iron metabolism and improving erythropoiesis efficiency, while the Hb response rate and safety of the two groups were comparable. This finding suggests that DA may provide better anemia management by more effectively inhibiting hepcidin and improving iron utilization, and also emphasizes the importance of comprehensive consideration of iron status when selecting EPO regimen.

In this study, the DA group had a greater reduction in serum hepcidin levels than the EPO-β group (-45.45 ± 22.67 vs. -30.11 ± 18.42 ng/mL, P < 0.001), corresponding to a 51.64% reduction in hepcidin levels compared with 35.75% in the EPO-β group (P < 0.001). This finding is in line with recent studies that show long-acting ESAs have more lasting hepcidin suppression. A network meta-analysis by Yang et al. showed that long-acting ESAs are linked to greater hepcidin suppression than short-acting ones [17]. Takasawa et al. also found that long-acting ESAs cause a secondary decrease in hepcidin 5-7 days after administration, while short-acting ESAs only cause a short rise that goes back to baseline quickly [16]. The lasting hepcidin suppression seen with DA in this study may be due to its long half-life (about 25 hours after it is injected into the vein) and its ongoing activation of EPO receptors [21-23].

Based on the hepcidin suppression results, the DA group showed better changes in iron metabolism markers. The DA group showed significant improvements in iron metabolism markers, with a greater decrease in TSAT (-9.614 ± 8.727% vs. 3.074 ± 1.058%, P < 0.001), and a greater increase in serum iron (3.846 ± 1.288 vs. 2.159 ± 0.776 μmol/L, P < 0.001) compared to the EPO-β group. These results match how the hepcidin-ferroportin axis works. As Mansour et al. reviewed, hepcidin is the main controller of iron balance in the body. It does this by directly binding to ferroportin, which is the only way iron can leave cells [24]. When hepcidin binds to ferroportin, it causes ferroportin to break down, and this stops iron from being released from macrophages, liver cells, and gut cells [24]. This key process has also been talked about in more recent papers on iron metabolism [25, 26]. As demonstrated by Shoji et al., DA suppresses hepcidin-25 more potently than recombinant human erythropoietin, facilitating iron mobilization from body stores [21]. The mobilized iron is rapidly utilized by the bone marrow for erythropoiesis rather than remaining bound to transferrin, which explains the concurrent increase in serum iron and

Table 6. Hb response and erythropoietin resistance index

Parameter	EPO-β group	DA group	*P* value
Hb response rate (≥ 11 g/dL)	33/58 (56.9%)	24/37 (64.86%)	0.534
ESA dose (baseline)	123.800 ± 24.200 IU/kg	105.200 ± 36.600 IU/kg	-
ESA dose (week 12)	117.20 ± 20.54 IU/kg	82.400 ± 35.200 IU/kg	-
ERI (IU/g/dL)	10.580 ± 2.158	7.250 ± 3.106	< 0.001***

***P < 0.001 compared between the two groups. Hb: hemoglobin; EPO-β: Erythropoietin-β; DA: darbepoetin alfa; Hb: Hb; ESA: Erythropoiesis-Stimulating Agent; ERI: ESAs Resistance Index.

Table 7. Adverse events during treatment

Adverse event	EPO-β group (n = 64)	DA group (n = 41)
Hypertension	2 (3.1%)	1 (2.4%)
Arteriovenous fistula thrombosis	1 (1.6%)	1 (2.4%)
Headache	1 (1.6%)	0 (0%)
Nausea	1 (1.6%)	0 (0%)
Injection site reaction	2 (3.1%)	1 (2.4%)
Any adverse event	7 (10.9%)	3 (7.3%)
Severe adverse event	0 (0%)	0 (0%)

EPO-β: Erythropoietin-β; DA: darbepoetin alfa

decrease in TSAT. This interpretation is supported by the significantly lower ERI observed in our DA group, confirming enhanced erythropoietic iron utilization. By lowering hepcidin, long-acting ESAs like DA help move iron out of storage places and make more iron available for making red blood cells [17]. Although there was no significant difference in ferritin levels between the two groups (P = 0.576), it can be observed that at week 12, ferritin levels in the DA group were significantly lower than those in the EPO-β group (302.5 vs. 352.5 ng/ml, P = 0.024). This may be due to the shorter follow-up time. It may be possible to observe the difference in ferritin changes over a longer follow-up period.

The results showed that the Hb levels of the two groups showed an upward trend during the treatment period, but there was no significant difference between the groups at each time point (all P > 0.05). This finding is consistent with the existing literature evidence. A meta-analysis of 16 randomized controlled trials (4,983 dialysis patients) conducted by Pérez-Ruixo et al. showed that there was no significant difference in the average Hb level of different ESAs (including short-acting EPO and long-acting DA) during the maintenance treatment stage, and the inter-individual variation of Hb was not associated with the type of ESAs, frequency of administration and route of administration [27]. In this study, the rate of Hb increase in the two groups was consistent with the classical Hb response characteristics of ESA summarized by Oberhoff et al. [28], and was consistent with the results of phase III clinical trials [29], which verified that there was no significant difference in Hb elevation effect of different dosage forms of ESAs. Cochrane systematic review [30] and Liu et al. [29] also further confirmed that there was no clinical significance difference between long-acting and short-acting ESAs in final Hb levels. It is worth noting that there was no significant difference in ΔHb between the two groups in this study (P = 0.614), which further supported the above conclusion. Although the mean increase in hemoglobin (ΔHb) was comparable between the two groups, the DA group exhibited substantially greater inter-individual variability, suggesting that while DA is effective at the population level, individual patients may exhibit considerably different hemoglobin responses. The longer half-life of DA (approximately 25 hours) may amplify differences in drug absorption, metabolism, and dose conversion from previous ESAs. Patient-specific factors such as baseline iron status, inflammatory state, and comorbidities may also contribute to this heterogeneity. Therefore, despite the convenience of less frequent dosing, clinicians should monitor hemoglobin more closely during the initial phase of DA treatment and adopt individualized dose adjustment strategies to optimize therapeutic outcomes.

The correlation analysis showed that significant correlations were observed between hepcidin changes and changes in iron metabolism markers. LnΔhepcidin showed a positive corre-

lation with LnΔFerritin (r = 0.285, P = 0.0029), LnΔTSAT (r = 0.234, P = 0.036), LnΔSerum iron (r = 0.307, P = 0.005) and LnΔHb (r = 0.250, P = 0.020). This result is in line with several recent studies. Fujikawa et al. found that Ln hepcidin-25 levels were positively correlated with mean corpuscular Hb, mean corpuscular Hb concentration, cholinesterase, serum iron, TSAT, Ln ferritin, and Ln hs-CRP in people on hemodialysis [11]. Similarly, Xu et al. showed that hepcidin levels were positively linked to ferritin and negatively linked to TSAT in people on long-term hemodialysis [12]. Li et al. [31] also confirmed these links. They found that iron markers play a part in the link between parathyroid hormone and EPO resistance, and hepcidin was behind about one-third of this link. The link between hepcidin and ferritin shows the control loop where hepcidin manages the release of stored iron [11, 16].

The results showed that the DA group demonstrated a significantly lower ERI (10.580 ± 2.158 vs. 7.250 ± 3.106 IU/g/dL, P < 0.001), indicating higher erythropoietic efficiency. This finding is consistent with the report by Pérez-García et al. who found that switching from epoetin alfa to DA was associated with a significant 23.9% reduction in the ERI at 24 weeks in patients requiring high ESA doses (P < 0.05), whereas patients who continued on epoetin alfa showed an increase in ERI over the same period [32]. Similarly, Molina et al. reported that the resistance index decreased significantly from week 8 after conversion to DA, further supporting the superior erythropoietic efficiency of long-acting ESAs [33]. Taken together, these findings, along with our results, suggest that DA offers better ESA responsiveness than short-acting epoetin formulations, likely due to its sustained EPO receptor activation and more efficient iron utilization.

Study limitations

Several limitations of this work should be acknowledged. First, the retrospective design may introduce selection and information bias. Second, the sample size was relatively modest, particularly in the DA group. Third, the 12-week observation period may be insufficient to capture long-term effects. Fourth, hepcidin measurement was limited to three time points, which may not fully characterize the dynamic response. Fifth, the study was conducted at a single center, which may limit generalizability. Prospective multicenter studies with larger sample sizes and longer follow-up periods are warranted to validate our findings. Future research should incorporate more frequent hepcidin measurements to better characterize the dynamic response to different ESA types, particularly during the early phase of treatment (e.g., daily measurements in the first week) to capture the biphasic hepcidin response.

Conclusions

This study demonstrates that DA is superior to EPO-β in suppressing hepcidin and modulating iron metabolism markers in maintenance hemodialysis patients, with higher erythropoietic efficiency despite comparable Hb response rates.

Disclosure of conflict of interest

None.

Address correspondence to: Yong Chen, Department of Pharmacy, Nanjing BenQ Medical Center, The Affiliated BenQ Hospital of Nanjing Medical University, No. 71 Hexi Street, Jianye District, Nanjing 210019, Jiangsu Province, China. Tel: +86-025-66863443; E-mail: cy15950535187@126.com

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