


Efficacy of Efepoetin Alfa for Chemotherapy-Induced Anemia in Breast Cancer Patients: Case Series

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ABSTRACT

Introduction: Anemia is a common complication among cancer patients and substantially reduces quality of life (QOL) through symptoms such as fatigue and cognitive impairment. This case evaluates the use of efepoetin alfa to treat chemotherapy-induced anemia (CIA) in late-stage breast cancer patients in Indonesia. **Case:** Six Asian women aged 43–59 years with stage III breast cancer receiving docetaxel-doxorubicin chemotherapy developed moderate anemia (mean baseline hemoglobin [Hb] 9.5 g/dL). Patients received subcutaneous efepoetin alfa (generally 0.3 mg/0.3 mL once); Hb was reassessed at an average of 8 days after the last injection. **Discussion:** Post-treatment mean Hb rose to 12.1 g/dL (mean ΔHb ≈ 2.6 g/dL). No serious adverse events were observed during the short follow-up. **Conclusion:** In this case, efepoetin alfa was associated with rapid increases in Hb and improved patient-reported outcomes; however, a confirmatory larger study, standardized dosing and monitoring, and longer follow-up are required to define efficacy and long-term safety.

Keywords: Anemia, breast cancer, case series, chemotherapy-induced anemia, efepoetin alfa.

ABSTRAK

Pendahuluan: Anemia merupakan komplikasi umum pada pasien kanker dan secara signifikan mengurangi kualitas hidup melalui gejala seperti kelelahan dan gangguan kognitif. Kasus ini mengevaluasi penggunaan efepoetin alfa untuk mengobati anemia yang disebabkan oleh kemoterapi pada pasien kanker payudara stadium lanjut di Indonesia. **Kasus:** Enam wanita Asia berusia 43–59 tahun dengan kanker payudara stadium III yang menerima kemoterapi docetaxel-doxorubicin mengalami anemia sedang (rata-rata hemoglobin [Hb] baseline 9,5 g/dL). Pasien menerima efepoetin alfa subkutan (umumnya 0,3 mg/0,3 mL sekali); Hb dievaluasi ulang rata-rata 8 hari setelah suntikan terakhir. **Diskusi:** Rata-rata Hb pasca-perawatan naik menjadi 12,1 g/dL (rata-rata ΔHb ≈ 2,6 g/dL). Tidak ada kejadian efek samping serius yang diamati selama masa tindak lanjut singkat. **Simpulan:** Dalam kasus ini, efepoetin alfa terkait dengan peningkatan cepat Hb dan perbaikan hasil yang dilaporkan pasien; namun, studi konfirmasi yang lebih besar, dosis dan pemantauan yang terstandarisasi, serta masa tindak lanjut yang lebih lama diperlukan untuk mendefinisikan efektivitas dan keamanan jangka panjang. **Zainal Abidin, Anova Fatimah. Efikasi Efepoetin Alfa untuk *Chemotherapy-Induced Anemia* pada Pasien Kanker Payudara: Serial Kasus.**

Kata Kunci: Anemia, kanker payudara, serial kasus, anemia yang diinduksi kemoterapi, efepoetin alfa.

INTRODUCTION

Anemia is a common and debilitating complication among cancer patients, severely impacting their quality of life (QOL) through symptoms such as fatigue, cognitive impairment, and general malaise.[1] In breast cancer patients, the prevalence of anemia can reach up to 41.1%.[2] Notably, approximately 50% of these patients are diagnosed at stage III, and around 17.9% undergo multiple chemotherapy regimens, which complicates the management of anemia even further.[2] The pathogenesis of cancer-related anemia is multifactorial, stemming from factors such as the cancer itself, associated comorbidities, blood loss, renal insufficiency, and the effects of myelosuppressive therapies.[1] Effective management of anemia is crucial, as it not only enhances treatment efficacy but is also linked to better survival rates and improved overall QOL for cancer patients.[1,3,4]

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Historically, red blood cell (RBC) transfusions have been the primary treatment for anemia, providing rapid symptomatic relief yet carrying risks such as infection transmission and transfusion-related complications.[5] To mitigate these risks, erythropoiesis-stimulating agents (ESAs) have emerged as alternative treatment options. Several ESAs are approved for managing chemotherapy-induced anemia (CIA) in the United States and certain European countries.[6–8] Furthermore, a number of guidelines have been published regarding the use of ESAs to treat CIA in cancer patients.[6,7,9]

In Indonesia, efepoetin alfa is developed by PT. Kalbe Genexine Biologics and is a long-acting erythropoietin hybrid Fc (hyFc®) fusion protein. It has demonstrated efficacy in stabilizing hemoglobin (Hb) levels and alleviating anemia-related symptoms, such as fatigue, in patients with pre-dialysis chronic kidney disease (CKD).[10] However, despite its success in CKD, this efepoetin alfa has not been comprehensively evaluated for cancer-related anemia in Indonesia and is not yet approved for this indication.

This case series aims to address this gap by evaluating the impact of Efepoetin alfa on Hb levels in breast cancer patients undergoing chemotherapy in Indonesia. By assessing the efficacy and safety of this novel ESA in a breast cancer population at high risk for anemia, we hope to provide valuable insights that could contribute to the development of more effective treatments for cancer-related anemia. Ultimately, our findings may inform health regulatory bodies in Indonesia regarding the use of ESAs for anemia treatment in cancer patients.

CASE SERIES

Patient Information

This case series adheres to the CARE (CAse REport) guidelines.[11] Ethical approval was not required according to local regulations; however, written informed consent was obtained from all individual patients for the publication of their anonymized data. We analyzed data from six Asian women, aged 43–59 years, all diagnosed with breast cancer in late 2023–early 2024. Their cancer stages ranged from stage 3A to stage 3B, with all patients successfully undergoing surgical interventions with minimal complications. Currently, each patient is receiving their first-line chemotherapy regimen, which consists of docetaxel 100 mg and doxorubicin 75 mg every 21 days. Reported concerns included fatigue and loss of appetite, particularly following chemotherapy cycles. Demographic and treatment data are summarized in **Tables 1 and 2**.

Table 1. Demographic data.

Patient	Age (Years)	Diagnosis	Diagnosis Since	Cancer Staging
A	59	Carcinoma mammae dextra	2024	cT3N1M0 stadium IIIA
B	58	Carcinoma mammae dextra	2024	cT4N2M0 stadium IIIB
C	43	Ulcerated carcinoma mammae sinistra	2023	cT4bN2bM0 stadium IIIB
D	49	Carcinoma mammae sinistra	2024	cT3N1M0 stadium IIIA
E	52	Ulcerated carcinoma mammae dextra	2023	cT4bN2aM0 stadium IIIB
F	47	Carcinoma mammae dextra	2024	cT3N2M0 stadium IIIA

Abbreviations: cT: Tumor size and extent (clinical assessment); N: Lymph node involvement; M: distant metastasis.

Table 2. Previous and current treatment.

Patient	Main Concerns and Symptoms	Previous Treatment	Chemotherapy Regiment	Cycle Planned
A	Fatigue, loss of appetite	Mastectomy dextra	Docetaxel 100, Doxorubicin 75	6
B	Fatigue, loss of appetite, diarrhea, nausea, mouth ulcers	Neoadjuvant chemotherapy (NAC) +Mastectomy dextra	Docetaxel 100, Doxorubicin 75	6
C	Fatigue, loss of appetite, diarrhea, nausea, mouth ulcers, fever	Neoadjuvant chemotherapy (NAC) + mastectomy sinistra	Docetaxel 100, Doxorubicin 75	6
D	Fatigue, loss of appetite	Mastectomy sinistra	Docetaxel 100, Doxorubicin 75	6
E	Fatigue, diarrhea, nausea, mouth ulcers, fever	Mastectomy dextra	Docetaxel 100, Doxorubicin 75	6
F	Fatigue, loss of appetite	Mastectomy dextra	Docetaxel 100, Doxorubicin 75	6


Clinical Findings and Diagnostics Assessment

This case series presents six patients who exhibited anemia following chemotherapy, characterized by clinical manifestations of fatigue, malaise, and pale appearance. Comprehensive laboratory evaluations revealed hemoglobin (Hb) levels below 12 g/dL, confirming the diagnosis of anemia. Differential diagnoses, including infections and electrolyte imbalances, were carefully ruled out, thereby establishing anemia as the primary contributor to the patients' symptoms.

According to the National Comprehensive Cancer Network (NCCN) guidelines, maintaining Hb levels above 10 g/dL prior to the initiation of chemotherapy is essential.[12] Consequently, a target Hb level of at least 10 g/dL was established for these patients.

To address the anemia, the attending physician prescribed Efepoetin alfa, an ESA, as a first-line intervention to enhance Hb levels. The decision to utilize efepoetin alfa over blood transfusions was made due to the potential risks associated with transfusions, which can include febrile reactions, hemolytic events, allergic responses, and iron overload. Such complications can adversely affect vital organ function and suppress the immune system.

Therapeutic Intervention

Efepoetin alfa was administered as the primary therapeutic intervention to elevate Hb levels. Each patient typically received 0.3 mg/0.3 mL efepoetin alfa subcutaneously, except one patient who received a higher dose of 0.6 mg/0.6 mL. Hb levels were initially planned for assessment three days post-injection; however, due to scheduling conflicts, the average time from the last injection to testing was around eight days. No dose adjustments were made. All patients tolerated efepoetin alfa well, with only mild injection site pain recorded as a common adverse effect. Importantly, no iron supplementation was provided to the patients; instead, all patients received a daily multivitamin, consumed once daily after meals. The composition of the multivitamin includes vitamin E 30 IU, vitamin C 750 mg, vitamin B1 HCL 15 mg, vitamin B2 15 mg, niacinamide 100 mg, vitamin B6 25 mg, vitamin B12 12 mcg, folic acid 0.4 mg, calcium (as calcium pantothenate and calcium carbonate) 20 mg, pantothenic acid (as calcium pantothenate) 20 mg, and zinc (as zinc sulfate heptahydrate) 20 mg. **Table 3** provides a summary of efepoetin alfa use for each patient.

OUTCOME

All six patients demonstrated a clinically significant increase in Hb levels, with pre-treatment averages of 9.5 g/dL rising to post-treatment averages of 12.1 g/dL, reflecting an average increase of 2.6 g/dL **(Table 3)**. Patients reported improved energy levels and overall well-being following the intervention. Follow-up diagnostic tests corroborated these increased Hb levels. Treatment adherence was monitored through regular follow-up visits and patient self-reports regarding side effects. In this case series, no side effects were reported regarding the use of efepoetin alfa.

DISCUSSION

Anemia is a prevalent and significant condition in cancer patients, particularly those undergoing chemotherapy. Studies estimate that approximately 40% of breast cancer patients experience anemia, with figures rising to 17% among those receiving multiple chemotherapy regimens.[2] The National Cancer Institute (NCI) classifies anemia by Hb levels into categories: mild (Hb 10.0 g/dL to the lower limit of normal), moderate (Hb 8.0–10.0 g/dL), severe (Hb 6.5–7.9 g/dL), and life-threatening (Hb < 6.5 g/dL).[9] Causes of anemia in cancer patients are multifactorial, encompassing the malignancy itself, blood loss, and side effects of treatments, particularly chemotherapy.[1] Among the repercussions of anemia, fatigue is a predominant symptom that significantly impairs the QOL of cancer patients, closely linked to the pathogenesis of cancer-related fatigue.[13]

In this case series, we presented outcomes from six Asian women diagnosed with breast cancer treated with efepoetin alfa for the management of CIA. These patients were undergoing chemotherapy regimens that included docetaxel and doxorubicin, with an average Hb level of 9.5 g/dL, indicative of moderate anemia prior to treatment. Fatigue was reported as the primary symptom by all patients, reinforcing findings from prior studies that delineate a significant association between

Table 3. Efepoetin alfa use.

Patient	Dosage	Frequency	Time from the Last Injection to Hb Testing (Days)	Hb Level Before (g/dL)	Hb Level After (g/dL)	Δ Hb (g/dL)
A	0.3 mg/0.3 mL	Once	9	10.1	13.5	3.4
B	0.3 mg/0.3 mL	Once	7	9.7	11.5	1.8
C	0.3 mg/0.3 mL	Once	19	9.1	10.6	1.5
D	0.3 mg/0.3 mL	Once	2	9.6	11	1.4
E	0.6 mg/0.6 mL	Once	3	8.6	12.6	4
F	0.3 mg/0.3 mL	Once	3	10	13.2	3.2
	Average		**8**	**9.5**	**12.1**	**2.6**


anemia and fatigue in cancer patients.[9] Notably, the incidence of CIA varies across different chemotherapy regimens, with around 18% of breast cancer patients treated with cyclophosphamide and docetaxel developing anemia, and this figure increases to as high as 60% among ovarian cancer patients undergoing carboplatin and paclitaxel treatments.[14] Moreover, patients with advanced cancer stages are at greater risk for developing anemia.

Efepoetin alfa was administered at a dose of 0.3 mg/0.3 mL via subcutaneous injection, with Hb levels assessed three days post-injection. The efficacy of ESAs, such as efepoetin alfa, is well-established, demonstrating improvements in Hb levels, reductions in the need for RBC transfusions, and enhancements in QOL for cancer patients. Current clinical guidelines recommend ESAs for moderate CIA (Hb 8.0–9.9 g/dL), RBC transfusions for severe CIA (Hb < 8 g/dL), and generally do not advocate for ESA use in mild CIA (Hb 10.0–11.9 g/dL).[6,7,9] For patients with identified iron deficiency, iron therapy is advised, alongside vitamin B12 or folate supplementation.[6] Although iron supplementation was not administered in this case series, the daily administration of a multivitamin containing vitamin B12 and folic acid may have positively influenced the recovery of Hb levels, suggesting that supportive care interventions alongside ESA treatment may enhance patient outcomes. Clinical guidelines indicate that Hb levels should be evaluated two weeks after the last injection for possible dose adjustments when Hb changes exceed 1 g/dL.[6] While our case series deviated from this recommendation—performing evaluations three days post-injection without dose adjustments—significant improvements in Hb levels were observed, rising from 9.5 g/dL pre-treatment to 12.1 g/dL post-treatment. This rapid response may signal the effectiveness of ESAs in addressing anemia, even when there are deviations from the guidelines. Patients reported enhanced energy levels and overall well-being, echoing existing literature that underscores the role of ESAs in improving QOL for anemic cancer patients, particularly when RBC transfusions present inherent risks due to potential infections and transfusion-related complications.[5]

While it is worth noting that no adverse effects related to the administration of efepoetin alfa were reported in this case series, it is essential to recognize the potential risks associated with ESAs. These risks include an increased likelihood of venous thromboembolism (VTE), hypertension, and mortality.[15,16] A Cochrane systematic review that analyzed 91 trials involving 20,102 participants found that although ESAs can decrease the need for RBC transfusions and improve quality of life, they are also linked to elevated risks of VTE, hypertension, and mortality.[15] This highlights the importance of carefully weighing the benefits against the risks, particularly for patients with advanced cancer or those at increased risk for thrombotic events.

Written informed consent was secured from all patients for the publication of anonymized data. Patient autonomy and welfare were prioritized throughout the treatment process, and our research adhered to ethical guidelines for case reporting. A significant ethical concern in implementing therapies like efepoetin alfa is ensuring equitable access. The high cost of ESAs can create barriers for patients in low-resource settings, emphasizing the need for solutions to provide equitable access to effective treatments for all patients, irrespective of socioeconomic status.

This case series is not without limitations. The small sample size of six patients restricts the generalizability of our findings, and the short follow-up period, with Hb levels assessed an average of eight days post-treatment, may not fully illuminate the long-term effects of Efepoetin alfa on CIA management. Further research involving larger sample sizes, extended follow-up durations, and ideally randomized controlled trials is necessary to validate the safety and efficacy of Efepoetin alfa in managing CIA.

In summary, while our case series demonstrates promising immediate outcomes following ESA administration, a more comprehensive investigation into the long-term implications and broader applicability is essential for establishing robust clinical management strategies for anemia in cancer patients. Continued exploration in this field remains vital for optimizing patient care and outcomes.

CONCLUSION

This case series underscores the significant impact of chemotherapy-induced anemia on the quality of life of breast cancer patients, particularly through fatigue. The use of efepoetin alfa showed promising short-term results, with increased hemoglobin levels and improved patient-reported energy and well-being, thereby supporting the efficacy of erythropoiesis-stimulating agents. However, the findings are tempered by the limitations of a small sample size and a short follow-up period, highlighting the need for larger studies and randomized controlled trials to evaluate the long-term safety and efficacy of efepoetin alfa. Furthermore, ensuring equitable access to such treatments for all patients remains a critical challenge in optimizing care. Ultimately, this research emphasizes the necessity for tailored management strategies to effectively address anemia in cancer patients, aiming to enhance care and outcomes for this vulnerable group.

Conflict of Interests

The clinician treating the patient in this case series has no affiliation with PT. Kalbe Genexine Biologics (KGBio), and no financial conflicts of interest related to the treatment provided.

Acknowledgement

The author acknowledges that article publishing charges were provided by PT. Kalbe Genexine Biologics (KGBio). Additionally, writing assistance for this article was provided by PT. Pharma Metric Labs.


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