JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Association of clinical factors with thrombocytopenia in patients receiving linezolid treatment: a retrospective study

Le Thi Phuong Thao[1 #], Nguyen Duc Trung[1], Le Thi My[1], Le Minh Hong[1], Bui Viet Hoan[2], Vu Quang Hung[2], Pham Dang Hai[2 #]

[1] Pharmacy Department, 108 Military Central Hospital, Vietnam
[2] Medical Intensive Care Unit, 108 Military Central Hospital, Vietnam

# Authors contributed equally to this work.

Abstract

Introduction: Linezolid (LZD) plays an important role in the treatment of severe infections caused by Gram-positive bacteria. Thrombocytopenia is regarded as one of the most common side effects of linezolid, which results from the destruction of platelets or myelosuppression**.** The study aimed to identify the risk factors associated with the development of thrombocytopenia in Vietnamese patients.
Methodology: This retrospective, descriptive cross-sectional study was performed on adult patients who received parenteral LZD therapy (1,200 mg/day) in at least 3 days between January 2020 and June 2021 at a tertiary referral hospital in Vietnam. Thrombocytopenia was defined as either a final platelet count of less than 100 G/L or a 25% decrease in platelet count from baseline. Multivariate logistic regression analysis was applied to predict risk factors associated with LZD-induced thrombocytopenia.
Results: In the 208 patients included in the study, the average age was 69 and males accounted for 73.1%. LZD-induced thrombocytopenia occurred in 37% of patients. LZD-induced thrombocytopenia was significantly associated with shock (HR = 8.26, 95% CI 3.82 – 17.84, $p < 0.001$), baseline creatinine clearance (HR = 1.02, 95% CI [1.01 – 1.03], $p = 0.002$), and duration of LZD treatment of at least 14 days (HR = 4.45, 95% CI [1.83 – 11.05], $p = 0.001$).
Conclusions: The results showed that thrombocytopenia was fairly common in patients using linezolid. Shock, renal failure, and duration of linezolid therapy of at least 14 days were significant risk factors for the incidence of linezolid-induced thrombocytopenia.

Key words: Linezolid; thrombocytopenia; Vietnam.

J Infect Dev Ctries 2024; 18(2):285-290. doi:10.3855/jidc.18488

(Received 05 May 2023 – Accepted 06 June 2023)

Introduction

Linezolid (LZD) belongs to the class of oxazolidinones which has been used in the treatment of severe infections caused by Gram-positive bacteria such as *Staphylococcus aureus* or vancomycin-resistant *Enterococcus faecium*. Linezolid binds to the 23S ribosomal RNA of the 50S subunit to impede protein synthesis of these bacteria [1]. The usual dose of linezolid in adults is 600 mg twice daily by oral or intravenous route. No adjustment of the linezolid dosage is needed in subjects with renal dysfunction [2,3]. Linezolid has been associated with hematological toxicity [3]. Thrombocytopenia is regarded as one of the most common side effects of linezolid, which results from the destruction of platelets or myelosuppression [4]. Previous studies conducted in Korea and Japan have reported some risk factors for linezolid-induced thrombocytopenia [5–9]. However, the data on Southeast Asian population is still unavailable. Therefore, the study aimed to identify the risk factors associated with the development of linezolid-induced thrombocytopenia in Vietnamese patients.

Methodology

Study design and population

This retrospective, descriptive cross-sectional study included hospitalized patients who received linezolid intravenously (600mg, q12h) for at least three consecutive days from January 2020 to June 2021 at a tertiary referral hospital in Vietnam.

The study excluded patients with a duration of linezolid therapy of fewer than three days or platelet counts of below 100 G/L before LZD initiation (Figure 1). Subjects who tested positive for viruses or had hematological diseases or lacked information from electronic medical records were ineligible.

Data collection

Data was collected from electronic medical records. Demographic and clinical characteristics included age, sex, comorbidity, mechanical ventilation, continuous renal replacement therapy (CRRT), hospital length of stay, septic shock and sources of infection, linezolid treatment duration, concurrent antibiotics, and baseline laboratory data (white blood cell, hemoglobin, C reactive protein (CRP), platelet count, serum creatinine) and microbiological isolates.

Baseline kidney function was calculated using the Cockcroft-Gault equation. The kidney functions were divided into 3 categories according to KDIGO guidelines: creatinine clearance (CrCL) > 60; 30 ≤ CrCL ≤ 60 and CrCL < 30 mL/min.

Thrombocytopenia definition

Thrombocytopenia was defined as either a final platelet count of less than 100 G/L or a 25% decrease in platelet count from baseline.

Statistical analysis

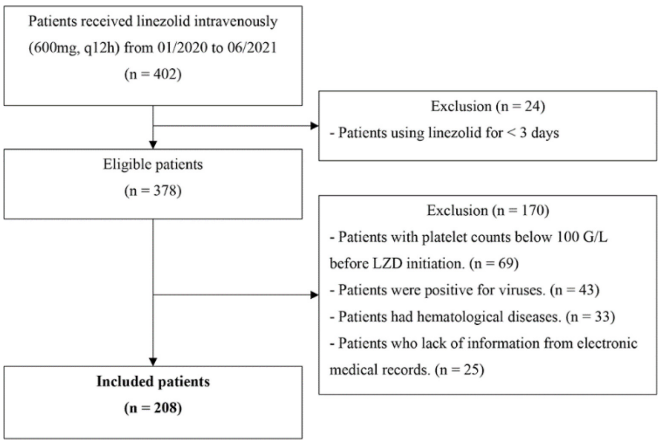
Statistical analysis was performed by SPSS version 21.0 and Epi info 7 software. Continuous variables were presented as mean values (standard deviation) for parametric variables and median (interquartile range) for nonparametric variables. Categorical variables were introduced as frequencies (percentages). Comparisons of continuous variables between groups based on the Student's *t*-test for normally distributed data and the Mann–Whitney *U* test for non-normally distributed data. Categorical variables were analyzed using the chi-square test or Fisher's exact test. Univariate and multivariate logistic regression analyses were applied to predict the factors related to the development of linezolid-induced thrombocytopenia. A *p* value of less than 0.05 was considered to be statistically significant.

This study was approved by the Institutional Review Board of 108 Military Central Hospital. Informed consent was not required for this study.

Results

A study was conducted between January 2020 and June 2021, where 402 consecutive adult patients were given LZD. However, 194 patients were excluded from the study due to various reasons. Among the excluded patients were 24 patients who used LZD for less than three days, 69 patients with platelet counts below 100 G/L before LZD initiation, 43 patients who were positive for viruses, 33 patients with hematological diseases, and 25 patients who lacked information from electronic medical records.

Figure 1. Inclusion/exclusion flowchart for study subjects.



A total of 208 patients were included in the study, of which 77 (37%) patients developed thrombocytopenia. Demographic data, clinical data, laboratory data at baseline, co-morbidities, origin of infection, microbiological species, and concomitant medications were presented in Table 1.

The patient's median age was 69 years, and 152 patients (73.1%) were male. The rates of shock, mechanical ventilation, and in-hospital mortality were higher in the thrombocytopenia group than in the non-thrombocytopenia group (62.3% vs. 15.3%, 76.6% vs 32.8% and 41.6% vs 9.9%, respectively, $p < 0.001$). No significant difference in the duration of LZD treatment and hospital LOS was found between the two groups. However, 26 (33.7%) patients in the group of thrombocytopenia and 22 (16.7%) patients in the group of non-thrombocytopenia were treated with LZD for more than 14 days ($p = 0.005$).

The most common co-morbidities were hypertension in 103 patients (49.5%), type 2 DM in 62 patients (29.8%), heart failure in 41 patients (19.7%), kidney disease in 40 patients (19.2%), and stroke in 36 patients (17.3%). The number of patients diagnosed with heart failure, kidney disease, and stroke was significantly higher in the thrombocytopenia group than in the non-thrombocytopenia group ($p < 0.05$).

The median WBC was 13.5 G/L, the median Hb was 104 g/L and the median CRP was 99 mg/L. The baseline platelet and serum creatinine level were statistically different between the two groups (202 G/L vs. 278 G/L and 148 vs. 72 μmol/L respectively, $p < 0.001$). The median CrCl was 47.2 mL/min. The rate of CrCl < 30 mL/min in the thrombocytopenia group was significantly higher than in the non-thrombocytopenia group (48.0% vs 19.1%).

The main sources of infection were respiratory tract in 88 patients (42.3%), soft tissue in 36 patients

(17.3%), urinary tract in 18 patients (8.7%), abdomen in 9 patients (4.3%). MRSA was isolated in 56 specimens (26.9%).

Carbapenem was the most frequently prescribed medication with LZD (50.7%). The percentage of patients taking antifungals and unfractionated heparin in the thrombocytopenia group was higher than that in the non-thrombocytopenia group (15.6% vs. 6.9%, p = 0.04 and 16.9% vs 3.8%, p = 0.001, respectively).

Seven factors significantly associating with linezolid-induced thrombocytopenia were identified by univariate analysis, including age (p = 0.03), shock (p < 0.001), baseline creatinine (p < 0.001), baseline creatinine clearance (p < 0.001), duration of LZD treatment (≥ 14 days) (p = 0.006), concomitant use of

Table 1. Characteristics of patients treated with linezolid.

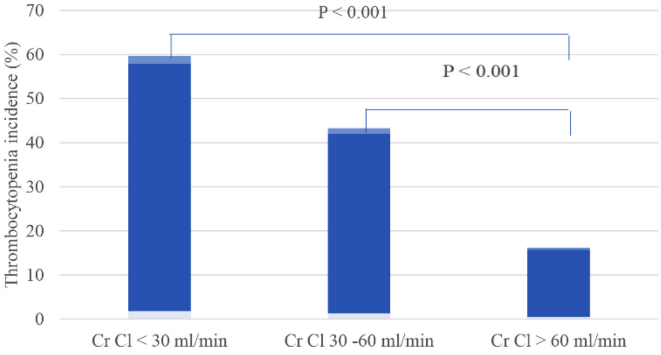
	All patients (n = 208)	Thrombocytopenia (n = 77)	Non-Thrombocytopenia (n = 131)	*p* value
Demographic data				
Age (years)	69 (57–79)	73 (59–82)	67 (55–77)	0.02
Male	152 (73.1)	52 (67.5)	100 (76.3)	0.17
Clinical data				
Shock	68 (32.7)	48 (62.3)	20 (15.3)	< 0.001
Mechanical ventilation,	102 (49.0)	59 (76.6)	43 (32.8)	< 0.001
Duration of LZD treatment (days)	9 (6–13)	10 (5–16)	9 (6–12)	0.20
Duration of LZD treatment (≥ 14 days)	48 (23.1)	26 (33.7)	22 (16.7)	0.005
Hospital LOS (days)	25 (17–39)	29 (18–47)	22 (16–37)	0.02
In-hospital mortality	45 (21.6)	32 (41.6)	13 (9.9)	< 0.001
Laboratory data at baseline				
WBC (G/L)	13.5 (9.5–19.1)	14.7 (10.8–20.7)	13.1 (9.2–18.2)	0.04
Platelet (G/L)	250 (182–343)	202 (159–273)	278 (204–382)	< 0.001
Hb (g/L)	104 (92–120)	101 (90–113)	104 (94–122)	0.22
Creatinine (µmol/L)	90 (59–209)	148 (89–286)	72 (53–122)	< 0.001
CRP (mg/L)	99 (42.2–147.2)	108 (80–223)	88.3 (43.7–146.0)	0.19
CrCl (mL/min)	47.2 (19.0–84.8)	30.1 (13.2–49.9)	64.3 (35.6–95.8)	< 0.001
< 30 mL/min	62 (29.8)	37 (48.0)	25 (19.1)	< 0.001
30 – 60 mL/min	60 (28.9)	26 (33.8)	34 (25.9)	
> 60 mL/min	86 (41.3)	14 (18.2)	72 (55.0)	
Co-morbidities				
Hypertension	103 (49.5)	44 (57.1)	59 (45.0)	0.09
Type 2 DM	62 (29.8)	27 (35.1)	35 (26.7)	0.2
Heart failure	41 (19.7)	23 (29.9)	18 (13.7)	0.005
Kidney disease	40 (19.2)	25 (32.5)	15 (11.5)	0.002
Stroke	36 (17.3)	21 (27.3)	15 (11.5)	0.004
Cancer	15 (7.2)	7 (9.1)	8 (6.1)	0.42
CRD	9 (4.3)	4 (5.2)	5 (3.8)	0.6
Liver disease	8 (3.9)	4 (5.2)	4 (3.1)	0.44
Alcohol abuse	2 (1)	1 (1.3)	1 (0.8)	0.7
Origin of infection				
Respiratory	88 (42.3)	32 (41.6)	56 (42.8)	0.86
Soft tissue	36 (17.3)	4 (5.2)	32 (24.4)	< 0.01
Urinary	18 (8.7)	9 (6.9)	9 (11.7)	0.23
Abdomen	9 (4.3)	1 (1.3)	1 (6.1)	0.09
Endocarditis	6 (2.9)	5 (6.5)	1 (0.8)	0.02
Catheter	5 (2.4)	2 (2.6)	3 (2.3)	0.89
Nervous system	3 (1.4)	1 (1.3)	2 (1.5)	0.89
Other	43 (20.7)	23 (29.9)	20 (15.3)	0.01
Microbiological species				
MRSA	56 (26.9)	19 (24.7)	37 (28.2)	0.58
Concomitant medications				
Carbapenem	105 (50.7)	45 (58.4)	60 (45.8)	0.08
Quinolones	49 (23.6)	21 (27.3)	28 (21.4)	0.33
Cephalosporins	45 (21.6)	16 (20.8)	29 (22.1)	0.82
Aminoglycosides	39 (18.8)	19 (24.7)	20 (15.3)	0.09
Piperacillin/ Tazobactam	12 (5.8)	6 (7.8)	6 (4.6)	0.34
Antihistamines	47 (22.6)	21 (27.3)	26 (19.9)	0.22
Antifungals	21 (10.1)	12 (15.6)	9 (6.9)	0.04
Unfractionated heparin	18 (8.7)	13 (16.9)	5 (3.8)	0.001
Clopidogrel	13 (6.3)	3 (3.9)	10 (7.6)	0.28
Aspirin	11 (5.3)	3 (3.9)	8 (6.1)	0.49
Anticonvulsants	11 (5.3)	4 (5.2)	7 (5.3)	0.96

Data are presented as median (interquartile range) for continuous variables, counts (%) (percentage) for nominal variables. CRRT: continuous renal replacement therapy; LZD: linezolid; LOS: length of stay; DM: diabetes mellitus; CRD: chronic respiratory disease; WBC: white blood cell; Hb: hemoglobin; CRP: C-reactive protein; CrCl: creatinine clearance (calculated by Cockcroft- Gault equation); MRSA:methicillin - resistant *Staphylococcus aureus.*

antifungals ($p = 0.049$), and unfractionated heparin ($p = 0.003$). These factors were selected for inclusion in the multivariate analysis, except baseline creatinine due to collinearity with baseline creatinine clearance. The variables finally associated with LZD-induced thrombocytopenia were shock (HR = 8.26, 95% CI 3.82–17.84, $p < 0.001$), baseline creatinine clearance (HR = 1.02, 95% CI [1.01–1.03], $p = 0.002$), and duration of LZD treatment ≥ 14 days (HR = 4.45, 95% CI [1.83–11.05], $p = 0.001$) (Table 2).

The incidence of thrombocytopenia in different groups of kidney functions was estimated (Figure 2). Thrombocytopenia occurred in patients in the group of CrCl < 30 mL/min, which was higher than that in the group of CrCl > 60 mL/min ($p < 0.001$).

Figure 2. Comparison of the thrombocytopenia incidence (%) according to kidney function.



CrCl: Creatinine clearance (calculated by Cockcroft – Gault equation)

Discussion

In our study, the proportion of patients experiencing LZD-induced thrombocytopenia was 37.0%. The rate of thrombocytopenia reported in the previous studies ranged from 13.8% to 53.2% [5–14]. Our results were similar to the incidence of LZD-induced thrombocytopenia that was reported by several studies previously conducted in Japan (38.6% in the study by Hirano *et al.* [7], 42% in the study by Natsumoto *et al.* [5] and 48.4% in the study by Hanai *et al.* [8]).

Reported risk factors of LZD-induced thrombocytopenia were low baseline platelet count, renal impairment, daily dose per weight, duration of treatment, combination with a carbapenem, and shock [5–14]. Following multivariate analysis, the factors associated with LZD-induced thrombocytopenia in our study were shock, baseline creatinine clearance, and duration of LZD therapy of more than 14 days. The duration of LZD therapy in this study followed the FDA-approved label of Zyvox®, which stated that linezolid-induced thrombocytopenia appears to depend on the duration of therapy, generally greater than 2 weeks [15]. The daily LZD dose per weight could not be assessed in our study because LZD was administered in a fixed dose manner at the hospital. Although low baseline platelet count and combination with a carbapenem were analyzed, associations of these factors with LZD-induced thrombocytopenia were not statistically significant. The study also evaluated the effect of concomitant medications which may cause low platelet count; however, no influence was observed.

Linezolid has been known to cause thrombocytopenia for decades, but the mechanism underneath is still unclear. Two responsible mechanisms were demonstrated [16]. The first one is myelosuppression, in which the drug molecules have a direct cytotoxic effect on the megakaryocytes, leading to dysfunctional thrombopoiesis within the bone marrow [17,18]. A study using rat platelet-rich plasma and human-immortalized cell lines suggested that LZD had no direct effect on platelet destruction, but rather induced thrombocytopenia via the suppression of platelet release from mature megakaryocytes [19]. Another study demonstrated that reductions in platelet counts were caused by the toxicity-induced suppression of platelet production by bone marrow and hematopoietic cells [20]. However, a bone marrow biopsy performed on a patient who experienced thrombocytopenia 7 days after starting linezolid

Table 2. Univariate and multivariate logistic regression analysis for linezolid induced thrombocytopenia.

Dependent variables	Univariable	*p*	Multivariable	*p*
	Hazard ratio (95% CI)		Hazard ratio (95% CI)	
Age	0.98 (0.96 – 0.99)	0.03	1.01 (0.99 – 1.03)	0.337
Male	0.64 (0.34 – 0.34)	0.168	-	-
CRRT	6.53 (3.31 – 12.87)	0.049		
Shock	9.18 (4.73 – 17.82)	< 0.001	8.26 (3.82– 17.84)	< 0.001
Baseline creatinine	9.18 (4.73 – 17.82)	< 0.001		
Baseline creatinine clearance	1.02 (1.01 – 1.03)	< 0.001	1.02 (1.01 – 1.03)	0.002
Duration of LZD treatment, (≥ 14 days)	2.52 (1.31 – 4.87)	0.006	4.45 (1.83 – 11.05)	0.001
Antifungals	2.50 (1.01 – 6.25)	0.049	1.33 (0.41 – 4.31)	0.637
Unfractionated heparin	5.12 (1.75 – 14.99)	0.003	2.50 (0.69 – 9.04)	0.161

CI: confidence interval; CRRT: continuous renal replacement therapy; LZD: linezolid; CrClr: creatinine clearance (calculated by Cockcroft – Gault equation).

revealed sufficient quantities of normal megakaryocytes [21]. This observation alone disproves the theory that thrombocytopenia is caused by a myelosuppressive mechanism and supports an immune-mediated mechanism of platelet destruction.

Among the independently associated risk factors of LZD-induced thrombocytopenia in our study, shock, and renal impairment can alter the pharmacokinetics of patients, hence increase the trough concentration of LZD. Cazavet *et al.* also proved that an elevated C_{min} of linezolid in plasma is a risk factor of LZD-induced thrombocytopenia [10]. Moreover, a study elucidating the underlying mechanism of linezolid-induced thrombocytopenia by using a chronic renal disease mouse model indicated that renal impairment decreased platelet counts *in vivo*.[4]. Renal impairment is a significant risk factor of LZD-induced thrombocytopenia in the previous studies [5,7,8,14]. In our study, we investigated the impact of renal function on platelet count by dividing the patient's renal function into 3 groups based on creatinine clearance before the treatment of LZD (Figure 2). The results showed that patients with moderate to severe renal impairment (CrCl < 60 mL/min) were more likely to suffer from thrombocytopenia. This finding is similar to the study of Hanai *et al.* [8]. Meanwhile, Choi *et al.* indicated that platelet count reduced significantly in patients with CrCl < 30 mL/min [14].

This is the first study investigating the incidence and risk factors of LZD-induced thrombocytopenia in the Vietnamese population. Besides the duration of LZD of more than 14 days which is labeled in the package insert, our results demonstrated that shock and renal impairment are also independently associated with LZD-induced thrombocytopenia. This study still has some limitations. Firstly, because data was collected from electronic medical records, we could not evaluate the influence of other factors on thrombocytopenia incidence due to lack of information. Secondly, since this is a retrospective study, we did not measure the linezolid concentration in the plasma. Thirdly, this is a single-center study, thus our results may not be generalized for all patients in Vietnam. However, our results did coincide with other studies in Asia, hence, wider validation should be carried out.

Conclusions

Thrombocytopenia is a common adverse effect of linezolid, an antibacterial medication used to treat various infections. Shock, moderate to severe renal insufficiency, and duration of linezolid therapy of more than 14 days were associated with thrombocytopenia. Therefore, in clinical practice, patients presenting those factors should be monitored closely for platelet counts to detect thrombocytopenia early.

References

1. Paterson DL, Pasculle AW, McCurry K (2013) Linezolid: the first oxazolidinone antimicrobial. Ann Intern Med 139: 863. doi: 10.7326/0003-4819-139-10-200311180-00017.
2. Brier ME, Stalker DJ, Aronoff GR, Batts DH, Ryan KK, O'Grady M, Hopkins NK, Jungbluth GL(2003) Pharmacokinetics of linezolid in subjects with renal dysfunction. Antimicrob Agents Chemother 47: 2775–80. doi: 10.1128/AAC.47.9.2775-2780.2003.
3. Birmingham MC, Rayner CR, Meagher AK, Flavin SM, Batts DH, Schentag JJ (2003) Linezolid for the treatment of multidrug-resistant, gram-positive infections: experience from a compassionate-use program. Clin Infect Dis 36: 159–68. doi: 10.1086/345744.
4. Nishijo N, Tsuji Y, Matsunaga K, Kutsukake M, Okazaki F, Fukumori S, Kasai H, Hiraki Y, Sakamaki I, Yamamoto Y, Karube Y, To H (2017) Mechanism underlying linezolid-induced thrombocytopenia in a chronic kidney failure mouse model. J Pharmacol Pharmacother 8: 8–13. doi: 10.4103/jpp.JPP_167_16.
5. Natsumoto B, Yokota K, Omata F, Furukawa K (2014) Risk factors for linezolid-associated thrombocytopenia in adult patients. Infection 42: 1007–12. doi: 10.1007/s15010-014-0674-5.
6. Ichie T, Suzuki D, Yasui K, Takahashi H, Matsuda M, Hayashi H, Sugiura Y, Sugiyama T (2015) The association between risk factors and time of onset for thrombocytopenia in Japanese patients receiving linezolid therapy: A retrospective analysis. J Clin Pharm Ther 40: 279–84. doi: 10.1111/jcpt.12260.
7. Hirano R, Sakamoto Y, Tachibana N, Ohnishi M (2014) Retrospective analysis of the risk factors for linezolid-induced thrombocytopenia in adult Japanese patients. Int J Clin Pharm 36: 795–9. doi: 10.1007/s11096-014-9961-6.
8. Hanai Y, Matsuo K, Ogawa M, Higashi A, Kimura I, Hirayama S, Kosugi T, Nishizawa K, Yoshio T (2016) A retrospective study of the risk factors for linezolid-induced thrombocytopenia and anemia. J Infect Chemother 22: 536–42. doi: 10.1016/j.jiac.2016.05.003.
9. Han X, Wang J, Zan X, Peng L, Nie X (2022) Risk factors for linezolid-induced thrombocytopenia in adult inpatients. Int J Clin Pharm 44: 330–8. doi: 10.1007/s11096-021-01342-y.
10. Cazavet J, Bounes FV, Ruiz S, Seguin T, Crognier L, Rouget A, Fourcade O, Minville V, Conil JM, Georges B (2020) Risk factor analysis for linezolid-associated thrombocytopenia in critically ill patients. Eur J Clin Microbiol Infect Dis 39: 527–38. doi: 10.1007/s10096-019-03754-1.
11. Attassi K, Hershberger E, Alam R, Zervos MJ (2002) Thrombocytopenia associated with linezolid therapy. Clin Infect Dis 34: 695–8. doi: 10.1086/338403.
12. Niwa T, Suzuki A, Sakakibara S, Kasahara S, Yasuda M, Fukao A, Matsuura K, Goto C, Murakami N, Itoh Y (2009) Retrospective cohort chart review study of factors associated with the development of thrombocytopenia in adult Japanese patients who received intravenous linezolid therapy. Clin Ther 31: 2126–33. doi: 10.1016/j.clinthera.2009.10.017.
13. Kaya Kılıç E, Bulut C, Sönmezer MÇ, Ozel Ö, Ataman Hatipoğlu Ç, Tuncer Ertem G, Tülek N, Kınıklı S (2019) Risk

factors for linezolid-associated thrombocytopenia and negative effect of carbapenem combination. J Infect Dev Ctries 13: 886–91. doi: 10.3855/jidc.10859.
14. Choi GW, Lee JY, Chang MJ, Kim YK, Cho Y, Yu YM, Lee E (2019) Risk factors for linezolid-induced thrombocytopenia in patients without haemato-oncologic diseases. Basic Clin Pharmacol Toxicol 124: 228–34. doi: 10.1111/bcpt.13123.
15. FDA (2013) Full prescribing information: ZYVOX® (linezolid) injection, tablets and oral suspension 2013: 1–25.
16. Loo AS, Gerzenshtein L, Ison M (2012) Antimicrobial drug-induced thrombocytopenia: A review of the literature. Semin Thromb Hemost 38: 818–29. doi: 10.1055/s-0032-1328882.
17. Bakchoul T, Marini I (2018) Drug-associated thrombocytopenia. Hematology Am Soc Hematol Educ Program 1: 576-583.
18. Aronson JK (2009) Meyler's Side Effects of Antimicrobial Drugs. 1st Edition. Elsevier Science.
19. Tajima M, Kato Y, Matsumoto J, Hirosawa I, Suzuki M, Takashio Y, Yamamoto M, Nishi Y, Yamada H (2016) Linezolid-induced thrombocytopenia is caused by suppression of platelet production via phosphorylation of myosin light chain 2. Biol Pharm Bull 39: 1846–51. doi: 10.1248/bpb.b16-00427.
20. Gerson SL, Kaplan SL, Bruss JB, Le V, Arellano FM, Hafkin B, Kuter DJ (2002) Hematologic effects of linezolid: Summary of clinical experience. Antimicrob Agents Chemother 46: 2723–6. doi: 10.1128/AAC.46.8.2723-2726.2002.
21. Bernstein WB, Trotta RF, Rector JT, Tjaden JA, Barile AJ (2003) Mechanisms for linezolid-induced anemia and thrombocytopenia. Ann Pharmacother 37: 517–20. doi: 10.1345/aph.1C361.

Corresponding author
Pham Dang Hai, MD, PhD
Medical Intensive Care Unit, 108 Military Central Hospital
No. 1 Tran Hung Dao street, Ha Noi, Vietnam.
Tel: +84987898960
E-mail: bsphamdanghai@gmail.com

Conflict of interests: No conflict of interests is declared.