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Spotlight on eltrombopag concentration in pediatric immune thrombocytopenia: A single-center observational study in China

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ABSTRACT

Importance: Eltrombopag has been recommended for pediatric immune thrombocytopenia (ITP). Response and adverse drug reactions (ADRs) varied widely between individuals, even at the same dose of eltrombopag. The appropriate eltrombopag concentration in ITP has not been reported.

Objective: This study aims to explore the appropriate eltrombopag concentration in pediatric ITP.

Methods: This was a single-center, prospective cohort study. Children diagnosed with refractory persistent/chronic ITP and platelet count $< 30\times10^9$/L were treated with eltrombopag and followed up for at least 2 months. Concentration was detected by high-performance liquid chromatography-mass spectrometry at least 2 weeks after eltrombopag. The clinical characteristics-concentration, concentration-response, and concentration-ADRs were analyzed.

Results: A total of 30 patients were enrolled, comprising 13 males and 17 females, with a median age of 72 (45–94) months. The median dose and concentration were 1.39 (1.09–1.56) mg/kg and 2.70 (2.25–4.13) mg/L, respectively. Of the enrolled patients, 14 responded to treatment, whereas 16 did not. Additionally, five experienced adverse drug reactions. No linear correlation was observed between eltrombopag concentration and clinical characteristics. The concentration was lower in the response group than in the nonresponse group, but there was no significant difference ($t = 0.755$, $P = 0.457$). Patients who experienced ADRs had a higher concentration than those without ADRs ($t = 2.538$, $P = 0.017$). The area under the receiver operating characteristic curve of ADRs was 0.78 (95% confidence interval: 0.56–1.00). Youden's index identified the cutoff point as 4.33 mg/L, with a sensitivity of 88% and a specificity of 60%. Logistic regression analysis demonstrated that a higher platelet count before eltrombopag predicted a favorable response.

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Interpretation: Eltrombopag proves efficacious and well-tolerated for treating pediatric ITP. However, prolonged and high-dose administration may increase the likelihood of ADRs. Thus, examining the appropriate eltrombopag concentration assists in directing individualized management of pediatric ITP.

KEYWORDS
Concentration, Efficacy, Eltrombopag, Immune thrombocytopenia, Pediatrics, Safety

INTRODUCTION

Primary immune thrombocytopenia (ITP) is the most common hemorrhagic disorder in childhood, with an annual incidence of 1.6–5.3 per 100 000.[1] Although most children with ITP have a good prognosis, 20%–30% will develop refractory persistent and chronic ITP, and mostly presents with mucocutaneous bleeding.[2] These children will suffer from a lousy quality of life and require second-line therapy. Though rituximab, splenectomy, dapsone, and thrombopoietin receptor agonists (TPO-RAs) have varied responses, all have been recommended as second-line therapy. However, TPO-RAs are being used increasingly for the treatment of ITP in adults as well as the pediatric population.

The pathogenesis of ITP is loss of immune tolerance to the autologous platelet antigen, which causes immune destruction of platelets and decreased platelet production by megakaryocytes.[3] TPO-RA could activate the TPO receptor and stimulate the JAK2/STAT5 pathway to increase megakaryocyte progenitor proliferation and platelet production.[4] Eltrombopag, as the earliest nonpeptide and small molecule oral TPO-RA, had been approved in many countries for treating pediatric ITP. International multicenter clinical studies and postmarketing studies in children have also confirmed its effectiveness and safety in treating ITP.[5–10] The updated international consensus report, along with the guidelines from the American Society of Hematology and adapted Chinese guidelines for children's ITP, suggest eltrombopag as a viable treatment for ITP.[1,11,12]

With the increasing use of eltrombopag, the importance of concentration is becoming more apparent, adverse drug reactions (ADRs), such as liver injury, skin pigmentation, and thrombocytosis may be related to higher plasma concentrations.[13,14] On the contrary, the lack of an increase in platelet count may be attributed to lower plasma concentration.[15,16] Although a practical cutoff value for concentration 2 h after eltrombopag administration in aplastic anemia has been reported, the appropriate concentration for ITP remains unclear.[15]

Especially, noteworthy is observed variability in the clinical responses and ADRs among individuals, even when administered the same dosage.[17,18] Currently, there is limited research on the clinical significance of eltrombopag concentration in patients with ITP in daily clinical practice. Thus, it is vital to investigate the optimal range and assess the significance of eltrombopag concentration in pediatric ITP.

METHODS

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the local Ethics Committee of Capital Medical University (approval number: [2023]-E-026-Y). Informed consent was obtained from all participants or their legal guardians included in the study.

Study patients

It was a single-center, prospective observational cohort study. All patients were enrolled between June 2022 and October 2022 from the Beijing Children's Hospital, Capital Medical University, Beijing, China.

Inclusion criteria: 1) Diagnosed with persistent or chronic ITP based on the Chinese adapted guidelines for pediatric ITP.[1] 2) Younger than 18 years old. 3) Failed to respond to glucocorticoid and intravenous immunoglobulin. 4) Platelet count should be less than $< 30\times10^9$/L prior to the initial eltrombopag dose. 5) Any measurements of the trough plasma concentration of eltrombopag should be obtained more than 2 weeks after dosimetric titration. 6) Patients should have a follow-up at least 2 months after dosimetric titration with the results for both efficacy and safety of eltrombopag.

Exclusion criteria: 1) Thrombocytopenia caused by other disorders, such as infection-related thrombocytopenia, hereditary thrombocytopenia, platelet agglutination

abnormality, connective tissue disease, aplastic anemia, and so on. 2) Bleeding score reached grade 4 according to the guidelines for rescue therapy.[1] 3) Children during the dose reduction period. 4) Abnormal liver function before the initial dose of eltrombopag.

Treatment and follow-up

All patients were given oral PROMACTA (eltrombopag) tablets, 25 mg per tablet.[19]

The initial dose of eltrombopag: 1.5 mg/kg per day for children aged 5 years or younger, 37.5 mg per day for children older than 5 years and with a weight < 27 kg, 50 mg per day for children older than 5 years and with a weight ≥ 27 kg.

Dosimetric titration: The dose will be adjusted according to the children's condition and drug instruction to maintain the platelet count range of (50–150)×10^9/L. The dose could be increased or decreased by 20% of the initial dose, and the maximum dose should not exceed 75 mg daily. Eltrombopag would be discontinued if the platelet count was exceeding 400×10^9/L. Each dose adjustment should be observed for at least 2 weeks to evaluate the platelet count thoroughly.

Follow-up: the concentration would be tested at least 2 weeks after the dose and oral time was stabilized. All patients would be followed up at least 2 months after the concentration testing, and the platelet count would be monitored at least every 2 weeks. Any ADRs would be recorded during this period.

Testing of eltrombopag concentration

Eltrombopag concentration was tested at least 2 weeks after the dose and oral time was stabilized. Blood samples were taken before medication to test the concentration. On the day of the blood draw, patients were asked to have blood drawn and then take eltrombopag under the supervision of the researchers to minimize the errors caused by time variation. Blood samples were drawn via the forearm vein into tubes containing K3-EDTA and were tested the same day. The protein precipitation method was used for sample pretreatment, Eltrombopag-13C4 was used as the internal standard, and a standard curve was established with the Eltrombopag reference standard. The concentration was assayed by Japer high-performance liquid chromatography-tandem mass spectrometry.[20] Analyst1.6.3 software was used for method establishment and result analysis.

Evaluation of outcomes

The response was defined as the number of platelet counts ≥ 50×10^9/L accounted for more than 75% of the total number of tests during the two-month follow-up period. Nonresponse was defined as the number of platelet counts ≥ 50×10^9/L accounted for less than 75% of the total number of tests during the follow-up period.

The grade and causality assessment with eltrombopag of adverse events were determined by two doctors according to the Common Terminology Criteria for Adverse Events (CTCAE) 5.0.[21] ADRs were defined as adverse events associated with eltrombopag.

Statistical analysis

All statistical analyses were performed using SPSS version 27.0 software. All figures were created using GraphPad Prism 9. Continuous data were described as the median and interquartile range (IQR). The *t*-test was used to compare data with normal distributions between groups, while the Mann–Whitney U test was used to compare data with non-normal distributions. Categorical data were described as the counts and percentages, and the chi-square test or Fisher's exact test was used to compare these data between groups. Spearman or Pearson correlation was used to explore the linear correlation between concentration and other variables. If a statistically significant difference in concentration was observed between the groups, receiver operating characteristic (ROC) curves were conducted to determine a concentration threshold associated with efficacy or ADRs. The best threshold was chosen by Youden's index. Logistic regression analysis was used to adjust for potential confounding factors. All statistical analyses were two-tailed, and $P < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

A total of 47 patients diagnosed with ITP were treated with eltrombopag and provided concentration results, but 17 patients who underwent dose reduction were excluded. In the final analysis, 30 patients (13 males and 17 females) were included, with a median age of 72 (45–94) months and a weight of 25.0 (16.8–30.5) kg. All patients had been treated with 2–6 drugs and had no response, including intravenous immunoglobulin, glucocorticoid, rituximab, immunosuppressors, and other TPO-RAs (recombinant human thrombopoietin, herombopag, or avatrombopag). The median course of ITP before eltrombopag was 22 (9–36) months, and the median platelet count before eltrombopag was 15 (10–20)×10^9/L. All the baseline clinical characteristics are shown in Table 1.

Application of eltrombopag

The initial doses of eltrombopag were determined by the age and weight of patients, and the doses were adjusted according to the children's condition and drug instruction to maintain the platelet count range from 50×10^9/L to 150×10^9/L. By detecting concentration, the median

TABLE 1 Clinical characteristics of patients

Clinical characteristics	Patients ($n = 30$)
Gender	
Male	13 (43.3)
Female	17 (56.7)
Weight (kg)	25.0 (16.8, 30.5)
Age (month)	72 (45, 94)
Previous treatment	
intravenous immunoglobulin	30 (100.0)
Glucocorticoid	30 (100.0)
Rituximab	18 (60.0)
Other TPO-RAs	4 (13.3)
Immunosuppressors	2 (6.7)
Kinds of previous treatment	3 (3, 4)
Course before eltrombopag (month)	22 (9, 36)
Platelet count before eltrombopag ($\times 10^9$/L)	15 (10, 20)
Eltrombopag at the time of plasma concentration	
Months from eltrombopag started	1.4 (0.5, 4.6)
Weeks with the current dose	3.8 (2.0, 10.2)
Dose per weight (mg/kg)	1.39 (1.09, 1.56)
Trough plasma concentration (mg/L)	2.70 (2.25, 4.13)
Effect of eltrombopag	
Response	14 (46.7)
Non-response	16 (53.3)
ADRs of eltrombopag	
Thrombocytosis	3 (10.0)
Elevated transaminase	2 (6.7)

Data are presented as *n* (%) or median (IQR).
Abbreviations: ADRs, adverse drug reactions; IQR, interquartile range; TPO-RAs, thrombopoietin receptor agonists.

duration from eltrombopag start was 1.4 (0.5–4.6) months, and the median duration with the current dose was 3.8 (2.0–10.2) weeks. The median prescription dose was 1.39 (1.09–1.56) mg/kg at the time of detection. Of the 30 patients, 14 (46.7%) had a response, and another 16 (53.3%) had no response to eltrombopag. Due to a smaller dose of eltrombopag in ITP, the incidence rate and severity of ADRs were lower in patients with ITP. Only five patients had ADRs, including three (10.0%) with increased platelet counts and two (7.3%) with elevated transaminase. All ADRs were grade 1 according to CTCAE 5.0. The details are shown in Table 1.

Linear correlations between clinical characteristics and concentration

The median concentration of eltrombopag was 2.70 (2.25–4.13) mg/L. Potential clinical characteristics that might influence concentration were collected and analyzed using the Spearman or Pearson correlation analysis. No linear correlation was found between clinical characteristics and eltrombopag concentration. The details are shown in Table 2.

TABLE 2 Exploration of linear correlations between clinical characteristics and eltrombopag concentration

Covariate	Correlation coefficient	*P*
Weight (kg)	0.145	0.445‡
Age (month)	0.079	0.680†
Kinds of previous treatment	−0.011	0.956‡
Course before eltrombopag (month)	−0.166	0.380‡
Platelet count before eltrombopag ($\times 10^9$/L)	−0.060	0.751†
Months from eltrombopag started	0.027	0.889‡
Weeks with the current dose	−0.035	0.855‡
Dose per weight (mg/kg)	0.087	0.646†

†Pearson correlation;
‡Spearman correlation.

Comparison of concentration between the response/ADR groups

Of the 30 patients, 14 (46.7%) responded to eltrombopag with a median concentration of 2.55 (1.97–3.89) mg/L, while 16 (53.3%) did not respond with a median concentration of 3.00 (2.53–4.18) mg/L. There was no significant difference observed in concentration between both groups ($t = 0.755$, $P = 0.457$) (Figure 1).

There were five (16.7%) patients with ADRs, who had a higher median concentration of 4.45 (2.65–6.05) mg/L, compared with 2.60 (2.05–3.80) mg/L for those without ADRs ($t = 2.538$, $P = 0.017$) (Figure 1). ROC curves were created to search for the cutoff values associated with ADRs (Figure 2). The area under the ROC curve of ADRs was 0.78 (95% confidence interval [95% CI]: 0.56–1.00). The specificity of ADRs increased and the sensitivity decreased with increasing concentration. Youden's index identified the cutoff point as 4.33 mg/L, with 88% of sensitivity and 60% of specificity.

Factors associated with response/ADRs of eltrombopag

Logistic regression analysis was used to identify the clinical characteristics influencing the response and ADRs of eltrombopag. Due to the small number of patients, univariate analyses with a *P*-value less than 0.200 were included in the following Logistic regression analysis. In the univariate analysis of the factors associated with the response to eltrombopag, the *P*-value of age, kinds of previous treatment, platelet count before eltrombopag, and month from

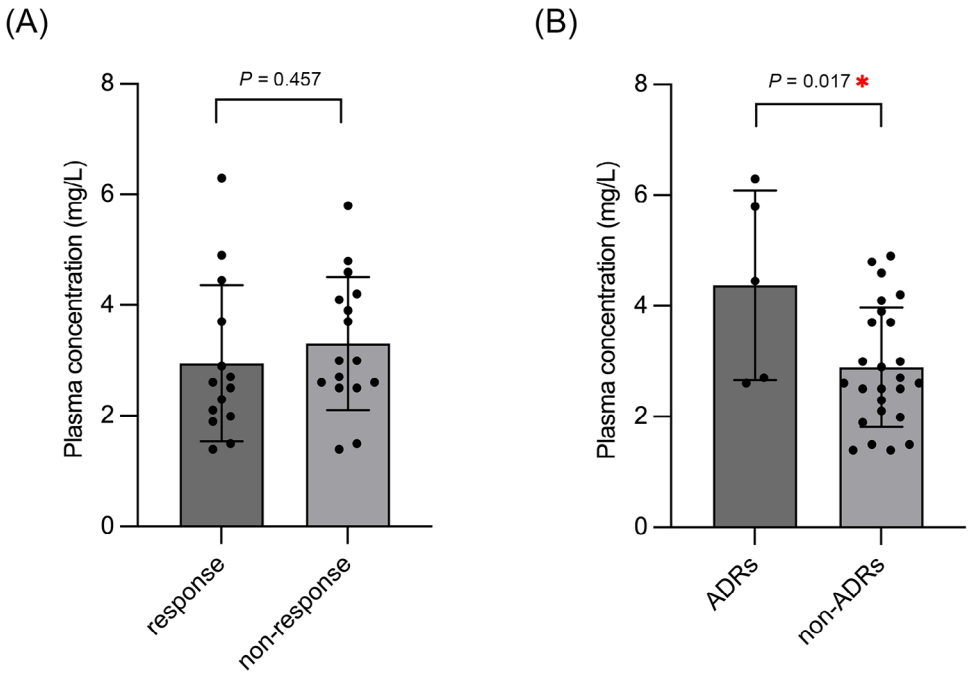

FIGURE 1 Comparison of eltrombopag through plasma concentrations between groups. (A) The trough plasma concentration showed no significant difference between the response and nonresponse groups ($t = 0.755$, $P = 0.457$). (B) The trough plasma concentration was significantly higher in the ADRs group than in the non-ADRs group ($t = 2.538$, $P = 0.017$). ADRs, adverse drug reactions.

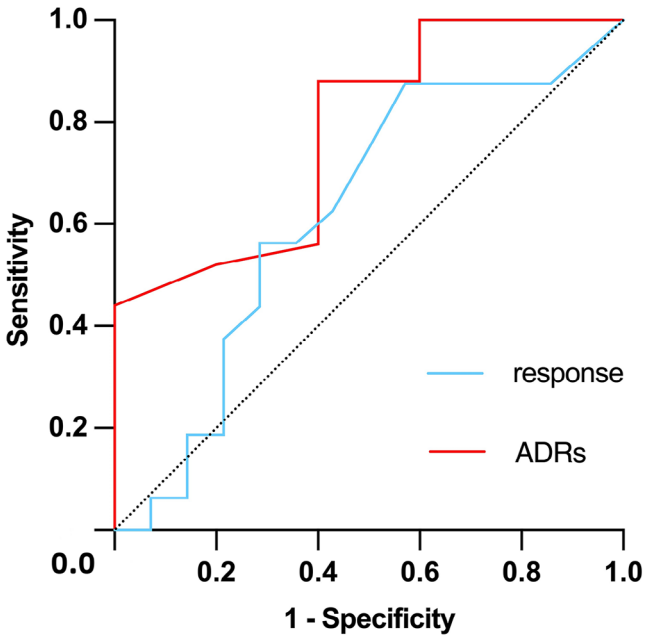

FIGURE 2 Receiver operating characteristics (ROC) curves for the trough plasma concentration of eltrombopag with the response and adverse drug reactions (ADRs). The area under the ROC curve of response was 0.62 (95% confidence interval [CI]: 0.41–0.83), with no significant correlation. The area under the ROC curve of ADRs was 0.78 (95%: CI 0.56–1.00), and Youden's index identified the cutoff point as 4.33 mg/L, with 88% of sensitivity and 60% of specificity.

eltrombopag start were less than 0.2. Logistic regression analysis of the four factors showed only a significant difference in platelet count before eltrombopag, with a *P*-value of 0.021 (Table 3). In the univariate analysis of the factors associated with the ADRs of eltrombopag, the *P*-value of months from eltrombopag started, weeks with the current dose and trough plasma concentration were less than 0.200, while months from eltrombopag started with a *P*-value of 0.015 and trough plasma concentration with a *P*-value of 0.017. However, after the logistic regression analysis, the difference was not observed for these three variables (Table 4).

DISCUSSION

Eltrombopag, as the earliest nonpeptide and small molecule oral TPO-RA, its efficacy and safety have been confirmed in the treatment of ITP.[5–10] Many authorities recommend eltrombopag as a treatment for ITP.[1,11,12] With the widespread use of eltrombopag, the value of the drug concentration is becoming more apparent. Some studies indicate that insufficient concentration may impact the efficacy of eltrombopag. Zuo et al.[15] discovered that the risk of eltrombopag inefficacy in aplastic anemia at a concentration between 11.2 and 15.2 μg/ml was 0.028-fold ($P = 0.041$) of that at a concentration between 3.2 and 7.2 μg/ml in a prospective and longitudinal cohort study.

TABLE 3 Univariate and multivariate analyses of factors associated with the response of eltrombopag

Covariate	Univariate analysis			Logistic regression analysis	
	Response ($n = 14$)	Non-response ($n = 16$)	*P*	OR (95% CI)	*P*
Gender			1.000†		
Male	6 (20.0)	7 (23.3)			
Female	8 (26.7)	9 (30.0)			
Weight (kg)	25.5 (20.5, 39.0)	21.5 (15.5, 29.3)	0.212‡		
Age (month)	90 (64, 96)	64 (37, 91)	0.140‡	1.027 (0.991–1.064)	0.140
Kinds of previous treatment	3 (2, 4)	4 (3, 5)	0.155‡	0.803 (0.326–1.974)	0.632
Course before eltrombopag (month)	22 (18, 33)	18 (4, 36)	0.417‡		
Platelet count before eltrombopag ($\times 10^9$/L)	20 (15, 28)	11 (6, 16)	0.002§	1.217 (1.030–1.439)	0.021
Months from eltrombopag started	2.4 (0.5, 6.1)	0.9 (0.5, 3.4)	0.196‡	1.063 (0.832–1.360)	0.624
Weeks with the current dose	4.7 (2.2, 11.8)	3.8 (2.0, 11.7)	0.517‡		
Dose per weight (mg/kg)	1.26 (1.03, 1.51)	1.47 (1.19, 1.60)	0.251§		
Trough plasma concentration (mg/L)	2.55 (1.97, 3.89)	3.00 (2.53, 4.18)	0.457§		

Data are presented as *n* (%) or median (IQR).
Abbreviations: CI, confidence interval; OR, odd ratio.
†Fisher's exact test.
‡Mann–Whitney *U* test.
§*t*-test.

TABLE 4 Univariate and multivariate analyses of factors associated with adverse drug reactions of eltrombopag

Covariate	Univariate analysis			Logistic regression analysis	
	ADRs ($n = 5$)	Non-ADRs ($n = 25$)	*P*	OR (95% CI)	*P*
Gender			1.000†		
Male	2 (6.7)	11 (36.7)			
Female	3 (10.0)	14 (46.7)			
Weight (kg)	30.0 (16.3, 43.8)	25.0 (16.5, 29.0)	0.486‡		
Age (month)	74 (33, 95)	69 (49, 95)	0.498§		
Kinds of previous treatment	3 (3, 4)	3 (3, 5)	0.795‡		
Course before eltrombopag (month)	10 (6, 23)	22 (10, 36)	0.242‡		
Platelet count before eltrombopag ($\times 10^9$/L)	14 (12, 29)	15 (8, 20)	0.437§		
Months from eltrombopag started	7.2 (2.0, 12.1)	0.9 (0.5, 3.6)	0.015‡	1.669 (0.737–3.783)	0.220
Weeks with the current dose	6.0 (3.8, 22.9)	3.0 (2.0, 11.3)	0.146‡	1.001 (0.827–1.211)	0.993
Dose weight (mg/kg)	1.25 (1.00, 1.59)	1.44 (1.09, 1.56)	0.523§		
Trough plasma concentration (mg/L)	4.45 (2.65, 6.05)	2.60 (2.05, 3.80)	0.017§	2.558 (0.693–9.440)	0.159

Data are presented as *n* (%) or median (IQR).
Abbreviations: ADRs, adverse drug reactions; CI, confidence interval; OR, odd ratio.
†Fisher's exact test.
‡Mann–Whitney *U* test.
§*t*-test.

Dionisi et al.[16] found that patients presenting a complete response showed augmented eltrombopag exposure parameters compared to subjects with partial or no response in ITP. However, excessive plasma concentration or prolonged exposure to eltrombopag may result in ADRs. For instance, a 3-year-old girl from Europe, with chronic ITP, experienced acute liver damage after using eltrombopag for 6 months with a concentration of 387.5 μg/ml. The patient fully recovered after stopping eltrombopag.[13] Another case was reported of a 57-year-old female from China with

chronic ITP who developed reversible hyperpigmentation after several months of treatment with eltrombopag.[14] In addition, Zuo et al.[15] found that an elevated risk of ADRs might be correlated with eltrombopag concentration. Furthermore, the plasma concentration of eltrombopag, which may be affected by gender, age, race, concomitant drugs, and other factors, has a great individual variation.[17,18] Therefore, it is vital to explore the appropriate range and factors that affect eltrombopag concentration in ITP.

A total of 30 patients were enrolled in this study, of whom fourteen exhibited response and five experienced ADRs. With regard to the effectiveness of eltrombopag, response was measured as the number of platelet counts$\geq 50\times10^9$/L accounted for more than 75% of the total number of tests performed. This approach took into account all platelet count tests carried out in the two-month follow-up period, thus providing a sustained response rate to eltrombopag and avoiding the bias caused by assessment at a set time. Due to the lower dose of eltrombopag used in pediatric ITP, the incidence rate and severity of ADRs were lower. Only five patients experienced ADRs, and all were classified as grade 1 according to CTCAE 5.0.

Previous research indicates that eltrombopag concentration could be influenced by various factors, such as gender, age, race, concomitant drugs, and so on.[17,18] However, none of these features was observed in this study, potentially due to our methodology. For example, we determined the dose of eltrombopag based on age and weight, taking into account that younger patients have a faster metabolism. As a result, the mean prescription dose of patients younger than 6 years old was significantly higher than patients older than 6 years old (1.56 mg/kg *vs*. 1.17 mg/kg, $t = 4.233$, $P < 0.001$), but their mean concentration exhibited no difference (3.06 mg/L *vs*. 3.21 mg/L, $t = -0.325$, $P = 0.748$). This result suggested that the eltrombopag concentration might be influenced by age.

Both univariate and multivariate analyses were used to analyze the correlation between response and eltrombopag concentration in ITP, but no significant difference was found. It was inconsistent with other studies, which might be because the efficacy of eltrombopag in ITP was affected by other factors.[15,16] ITP was an autoimmune-mediated disease, and whether patients got better mainly depended on the state of their immune systems. Drugs only played an auxiliary role in patients' recovery, so the effect of concentration was not as significant as expected. However, concentration might offer insight into determining the cause of ineffectiveness when administering an appropriate dose to patients with a high metabolism who require a higher dose of eltrombopag. In this study, other factors influencing the response or ADRs of eltrombopag were found. Patients with a higher platelet count before eltrombopag were more likely to reach response than patients with a lower platelet count in ITP, as evidenced by both *t*-test ($P = 0.002$) and logistic regression analysis ($P = 0.021$), suggesting that platelet count before eltrombopag played an essential role in response to eltrombopag.

ADRs were reported in many works of literature, including elevated transaminase, elevated bilirubin, headache, skin rash, nausea, fatigue, diarrhea, etc.[15,16] Pharmacokinetic studies demonstrated that the eltrombopag concentration was positively correlated with the rate of ADRs.[16,18,22] This was confirmed in our study that patients who experienced ADRs had significantly higher concentrations than those who did not ($t = 2.538$, $P = 0.017$). According to the ROC curve, the cutoff value for the concentration showing ADRs was 4.33 mg/L. However, this difference disappeared after logistic regression analysis, suggesting that the duration of eltrombopag might interfere with evaluating the effect of concentration on ADRs. Previous studies have shown that prolonged eltrombopag administration may cause a higher rate of ADRs, which is consistent with our study.[23]

For individuals with chronic disease, the aim of ITP treatment is to increase platelet counts to a safe level, minimize bleeding incidents, and enhance health-related quality of life (HRQoL) while minimizing ADRs.[24,25] During the treatment and management operations, personalized medicine should be prioritized, with consideration for patients' preferences and encouragement for their involvement in the decision-making process. Studies related to the treatment and management of chronic ITP showed, that both the early administration and prolonged use of effective and well-tolerated TPO-RAs have the potential to significantly control bleeding, decrease anxiety about the condition, reduce hospitalization and therapy costs, and improve HRQoL in patients with ITP.[26,27] Other studies showed the possible clinical benefit that can be obtained by combining conventional treatment with TPO-RAs, in terms of increased response rates and reduced mortality.[28] Among the various treatment modalities, patients have shown a preference for oral medications.[29] Therefore, in second-line treatment of ITP (rituximab, TPO-RAs, splenectomy, etc.), oral TPO-RAs are widely used and favored by patients.

There was no standard dose of eltrombopag for pediatric ITP. According to PETIT/PETIT2, Asian individuals received a lower initial dose due to their higher plasma eltrombopag exposures.[5,6] However, the U.S. Food and Drug Administration approval summary suggested pediatric patients of ages 1–5 years, regardless of ancestry, started at a dose of 25 mg daily.[19] Studies of Chinese adults have also shown that the median effective dose was the same as that of Europeans and Americans.[23,30] Therefore, we took the above-recommended doses as a reference and decided the dose in our study.

In clinical practice, eltrombopag dosage can be adjusted according to the platelet count and ADRs. However, due to the individual patient differences in eltrombopag demand, doctors need trial and error to achieve the ideal dose for each patient. This method requires patients to make frequent hospital visits and undergo blood samples, leading to discomfort, increased time expenditure, and financial burden. Adjusting eltrombopag dose according to concentration can expedite achieving the ideal dose more quickly to improve efficacy, reduce ADRs, and alleviate the economic burden of patients. Therefore, the plasma concentration could be a reference for individualized treatment of eltrombopag in pediatric ITP.

There were some limitations in this study, including the insufficient number of patients, which might affect many results. In addition, due to the low dose of eltrombopag in patients with ITP, only five patients experienced ADRs compared to 25 patients without ADRs, which may affect the results. Therefore, more trials with a larger sample size are needed to confirm our conclusion in the future.

Eltrombopag proves to be effective and well-tolerated for pediatric ITP. Long-term exposure and high concentration may lead to a higher risk of ADRs. Exploring the appropriate plasma concentration of eltrombopag is helpful in guiding the individualized treatment of pediatric ITP.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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