REVIEW ARTICLE

Efficacy and safety of eptinezumab for migraine: A systematic review and meta-analysis

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Background: Calcitonin gene-related peptides (CGRP) have been considered a new effective means to prevent and treat migraine. Eptinezumab is a new class of CGRP antagonists that has been ratified for clinical treatment. The purpose of this systematic review was to assess and contrast the therapeutic effect and safety of eptinezumab in the management of migraine in comparison with a placebo. **Materials and Methods:** We systematically searched PubMed, Embase, Cochrane Library, and the US National Institutes of Health Clinical Trials Registry from the earliest date to February 16, 2023, for randomized controlled trials (RCTs). The mean difference (MD) and risk ratio (RR) were chosen to assess clinical indicators. **Results:** In total, there were 2, 739 patients in four RCTs, who were ultimately included. Our summarized results showed that eptinezumab had better healing efficacy compared to placebo with respect to monthly migraine days (MD = −1.56, 95% confidence interval [CI]: −2.32, −0.79, $P < 0.001$), improving ≥75% migraine responder rate (RR = 1.80, 95% CI: 1.40, 2.33, $P < 0.001$), ≥50% migraine responder rate (RR = 1.46, 95% CI: 1.33, 1.61, $P < 0.001$), and 100% migraine responder rate (RR = 2.41, 95% CI: 1.08, 5.38, $P < 0.001$). Furthermore, compared with placebo, there was no significant increase for treatment-related adverse events (RR = 1.01, 95% CI 0.94, 1.10, $P = 0.71$) and serious AEs (RR = 0.93, 95% CI 0.46, 1.90, $P = 0.84$). It was found that all dosages except for 10 mg had significant efficacy compared with placebo, especially 300 mg ($P < 0.001$). **Conclusion:** Eptinezumab has good healing efficacy and insignificant adverse effects in treating migraine, particularly the dosage of 300 mg.

Keywords: Efficacy, eptinezumab, migraine, safety

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INTRODUCTION

Migraine is a usual chronic paroxysmal neurological disease associated with multiple episodes of headache associated with disruptions of neurological, gastrointestinal tract, and sensory functions.[1-4] Annually, approximately 2.5% of migraine patients worldwide switch from episodic to chronic migraine.[5] As one of the most disabling diseases in the world, migraine has caused significant social and economic impacts.[6] It has been proven as a very large adverse impact on the patients' quality of life, impairing work, and public activities.[7,8]

Preventive therapy plays a crucial part in improving the life quality of patients and preventing the progression of chronic migraine.[9] Currently, preventive treatment for migraine includes medications produced for conditions other than migraine (e.g., hypertension, depression, and epilepsy).[10-12] Calcitonin gene-related peptide (CGRP) was a kind of neuropeptide abundant in the trigeminal system. They have been proven to be widely expressed in both the peripheral and central nervous systems and emerged as a possible mechanism designed to prevent migraine attacks. In addition, they were the first specifically designed to function in the trigeminal neuralgia system with little adverse reaction.[13-17] Some

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studies indicated that the action of CGRP in migraine was mediated by modulating pain perception and maintaining neurogenic inflammation, resulting in increased peripheral and central sensitization.[18,19]

As a novel type of CGRP antagonist, eptinezumab has been endorsed as a new treatment option for preventing adult migraine in 2020.[20] In this meta-analysis, we collected patients' information and outcome indicators from screened randomized controlled trials (RCTs).[21-24] In this meta-analysis, we elucidated the healing effect and safety of eptinezumab by comparing different measures of migraine treatment outcomes. Simultaneously, the different dose was bound to bring different efficacy and safety; hence, subgroup analyses were performed to assess the distinction between various doses.

METHODS

Search strategy

The electronic databases PubMed, EMBASE, Cochrane Library, and the US National Institutes of Health Clinical Trials Registry were searched comprehensively in February 2023 for relevant articles. The following keywords are used in combination: migraine or chronic migraine, eptinezumab, and RCTs. Besides, we constrained systematic search to assure that the researches included were the most relevant.

Inclusion and exclusion criteria

All studies involved pursued the following inclusion and exclusion criteria: (a) type of research: RCT; (b) date and language constraint: no date and language constraints; (c) participant information restrictions: aged 18–75 years, no ethnicity restriction, no state restriction, <50 years of age with a period of migraine for at least 12 months, and 14 or more headache days per month. (d) intervention doses: placebo and eptinezumab at dosages of 10 mg, 30 mg, 100 mg, 300 mg, and 1000 mg. Besides, we removed protocols, case conferences, case reports, case reviews, and case comments.

Data extraction and quality assessment

We collected the following information from included researches: details in the trials involved (first research author, publication period, study Nation Clinical Trials (NCT) number, states, total duration, study design, and treatment arms), baseline and characteristics of included studies (age, sex, body mass index, monthly migraine, and number of days of headache per month), and outcome measures (migraine responder rate, monthly migraine days [MMDs], treatment-related adverse events [TEAEs], and serious adverse events [SAEs]). A subjective assessment of the methodological quality of the included studies was performed by two authors using the Cochrane Collaboration's tool for randomized studies.

Outcome measures

The main efficacy outcome indicators were compared: the mean difference (MD) of MMDs. Besides, ≥75%, ≥50%, and 100% migraine responder rates were compared separately as the secondary efficacy outcome. A decrease in the number of MMDs and rate of migraine responder were used to demonstrate the efficacy of eptinezumab. The primary safety outcome illustrated the risk ratio (RR) of participants who have experienced TEAEs or SAEs. In this study, a lack of TEAEs and SAEs had a positive result of the safety assessment.

Statistical analysis

In our research, the MD and RR were calculated for efficacy and safety comparison between studies. Random effects were applied throughout the analysis due to the heterogeneity in different studies. P <0.05 was considered statistically significant. Cochran's Q and heterogeneity index statistics were employed to assess the analysis of heterogeneity among trials.[25] If I^2 ≤50%, then the variation in the study was considered homogeneous. Conversely, If I^2 >50%, data comparison between trials was considered significantly heterogeneous, and a random-effects model was applied. A sensitivity analysis was conducted to check the robustness of the results. For the analysis of publication bias, funnel plots were used.[26] The meta-analysis was performed using Stata version 15.1 (Stata Corporation, College Station, Texas, USA).

RESULT

Study selection and study characteristics

A total of 418 articles were identified using the search strategy mentioned above through PubMed, Embase, and Cochrane Library, and 246 duplicate articles were excluded. One hundred and eighty-two studies were excluded for not being directly relevant; there were 64 articles remaining. Sixty studies were further excluded due to: 13 protocols, eight comments, 33 reviews, five conference abstracts, and one meta-analysis. Finally, we selected four studies for our meta-analysis. Altogether, 2, 739 participants from four RCTs were gathered. The specific article screening process is shown in Figure 1. The studies assessed both the therapeutic efficacy and security of eptinezumab, which was added at the doses of 10 mg, 30 mg, 100 mg, 300 mg, and 1000mg. Features in the screened researches are provided in Table 1. The characteristics of the participants are summarized in Table 2.

Primary efficacy outcomes

The primary efficacy outcome was the change from the baseline in the number of MMDs during weeks 1–12. The adjusted treatment difference was remarkable at any dose of the eptinezumab group in comparison to the placebo [MD = −1.56, 95% CI: −2.32, −0.79, P < 0.001

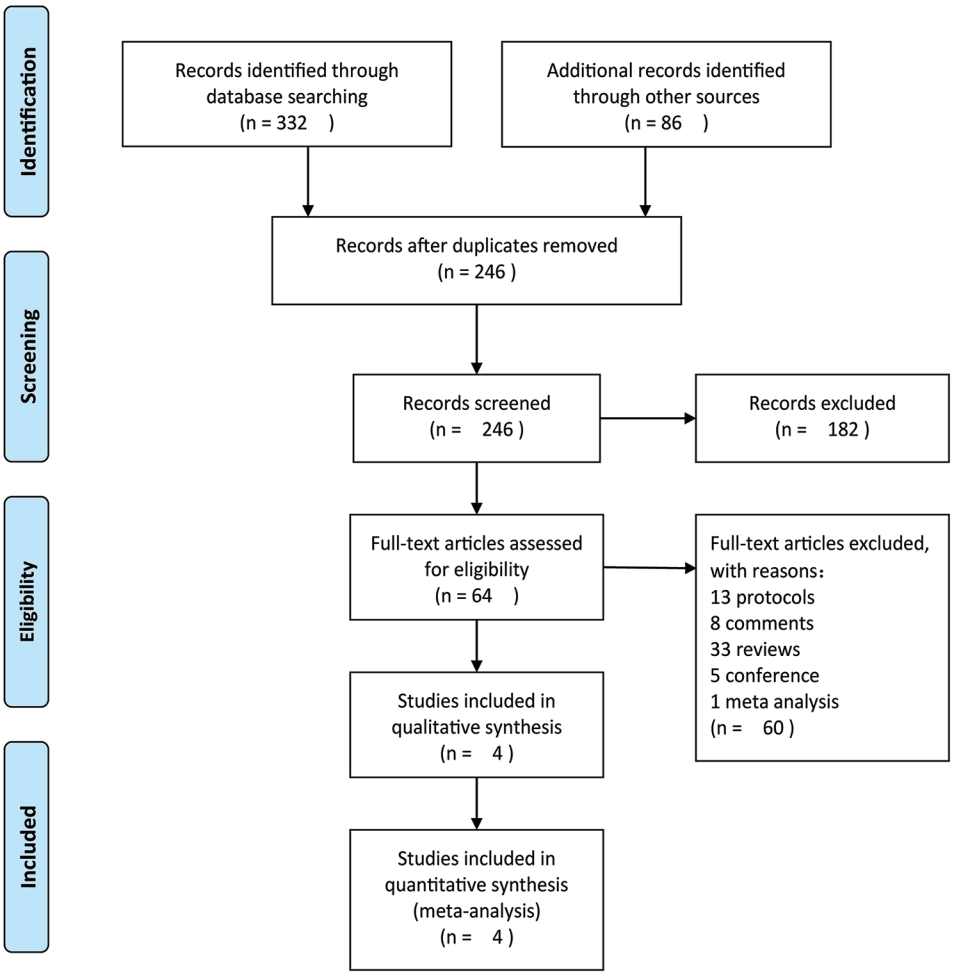

Figure 1: The study search, selection, and inclusion process

Table 1: Characteristics of the included studies

Study NCT number	Dodick 2014 (NCT01772524)[24]	Dodick 2019 (NCT02275117)[21]	Ashina 2020 (NCT02559895)[22]	Silberstein 2020 (NCT02974153)[23]
Study design	26 centers in the United States	92 sites in the United States, Australia, New Zealand, and Georgia	84 sites in the United States and Georgia	128 sites in 13 countries
Phase	III	III	III	III
Total duration (weeks)	24	49	60	36
Treatment arms	Placebo Eptinezumab 1000 mg	Placebo Eptinezumab 10 mg Eptinezumab 30 mg Eptinezumab 100 mg Eptinezumab 300 mg	Placebo Eptinezumab 30 mg Eptinezumab 100 mg Eptinezumab 300 mg	Placebo Eptinezumab 100 mg Eptinezumab 300 mg
Inclusion criteria	Age: 18–55 years Had a history of migraine ≥12 months Diagnosed before the age of 50 years were eligible for inclusion Had an estimated frequency of 5–14 migraine days per 28-day period in each of the 3 months before screening	Age: 18–55 years A diagnosis of migraine established at the age of 35 years and a history of migraine for 1 year Had 15 headache days, of which 8 were assessed as migraine days during the 28-day screening period	Age: 18–75 years Had a history of migraine ≥12 months With 14 headache days per month, including 4 migraine days, in the 3 months before screening	Age: 18–65 years Had a history of chronic migraine ≥12 months Experienced ≥15 to ≤26 headache days, including ≥8 migraine days, during the 28-day screening period
Exclusion criteria	Populations aged 75 years and older	Populations aged 75 years and older	Populations aged 75 years and older	Populations aged 75 years and older.

Figure 2a]. One subgroup analysis was performed to contrast the therapeutic efficacy of various eptinezumab dosages in MMDs, and curative effect of 300mg was the best, 10 mg (MD = −1.10, 95% CI: −2.79, −0.59, $P = 0.20$), 30 mg (MD

Table 2: Baseline of included studies

Study	Treatment arms	Age (range)	Women, *n* (%)	Mean (SD)		
				BMI (kg/m²)	Number of headache days	Number of migraine days
Dodick 2014[24]	Eptinezumab at a dose of 1000 mg (*n*=81)	38.6 (10.8)	67 (83)	N/A	9.2 (2.6)	8.4 (2.1)
	Placebo (*n*=82)	39.0 (9.6)	66 (80)	N/A	9.6 (2.8)	8.8 (2.7)
Dodick 2019[21]	Eptinezumab at the doses of 10 mg, 30 mg, 100 mg, and 300 mg (*n*=495)	36.5 (9.78)	426 (86)	27.42 (5.3)	21.2 (3.9)	16.5 (5.0)
	Placebo (*n*=121)	37.2 (9.2)	109 (90)	27.6 (5.9)	21.1 (4.1)	16.4 (5.1)
Ashina 2020[22]	Eptinezumab at the doses of 30 mg, 100 mg, and 300 mg (*n*=666)	39.8 (11.3)	563 (84.5)	29.4 (7.7)	10.1 (3.14)	8.67 (2.92)
	Placebo (*n*=222)	39.9 (11.67)	186 (83.8)	29.6 (7.28)	9.9 (2.83)	8.4 (2.68)
Silberstein 2020[23]	Eptinezumab at the doses of 30 mg, 100 mg, and 300 mg (*n*=706)	41.0 (11.06)	621 (88.0)	N/A	N/A	N/A
	Placebo (*n*=366)	39.6(11.28)	325 (88.8)	N/A	N/A	N/A

SD=Standard deviation; N/A=Not applicable; BMI=Body mass index

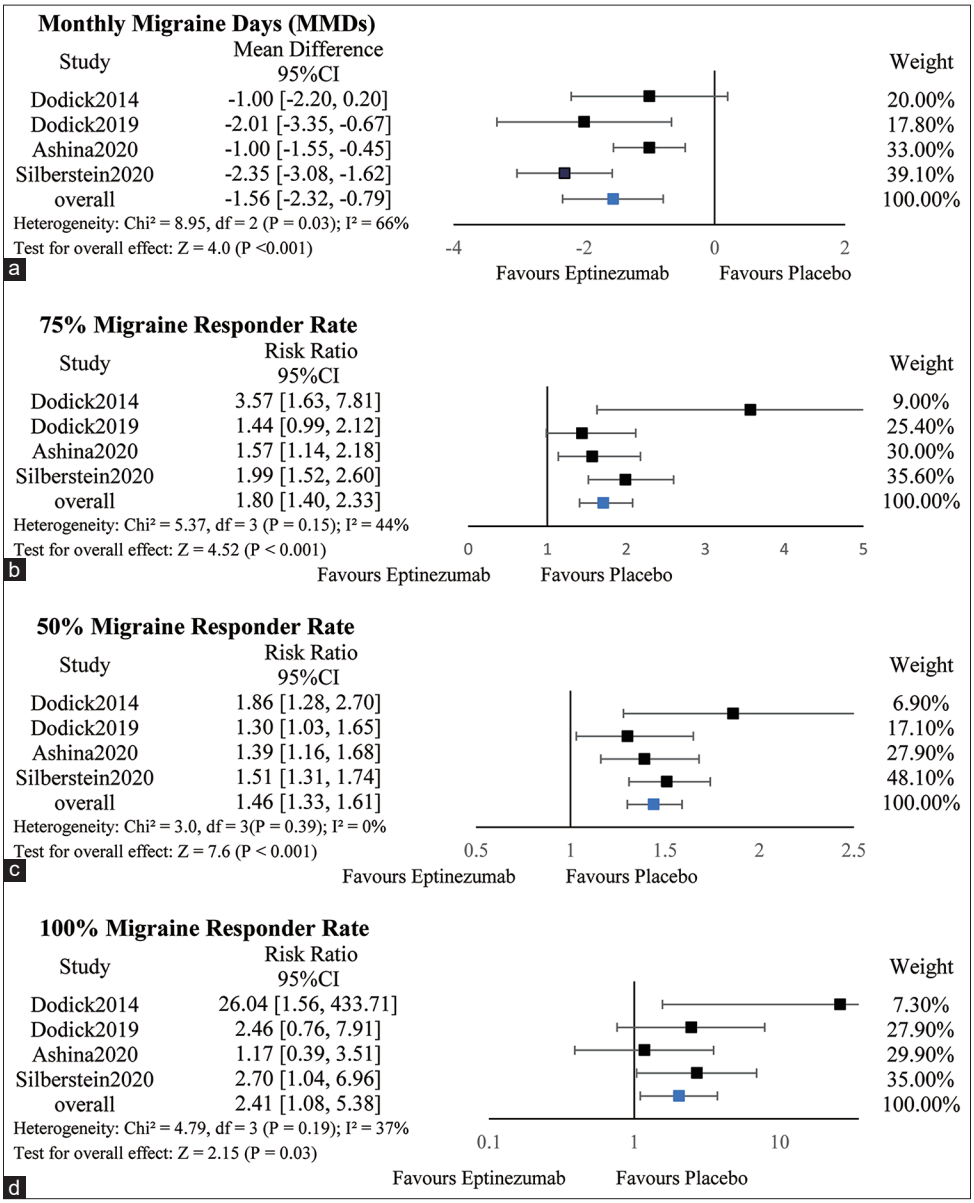

Figure 2: The pooled mean difference (MD) or risk ratio (RR) of efficacy outcomes of any-dose eptinezumab compared with placebo. Notes: The black squares indicate the estimated MD or RR for each randomized controlled trial (RCT), and the extending lines indicate the estimated 95% confidence interval (CI) of MD or RR for each RCT. Red squares indicate the estimated MD or RR (95% CI) for all patients. Weights are from a random-effects analysis. MD = Mean Difference; RR = Risk Ratio; CI = Confidence interval; RCT = Randomized controlled trial

= −1.42, 95% CI: −2.60, −0.23, $P = 0.02$), 100 mg (MD = −1.55, 95% CI: −2.57, −0.54, $P < 0.01$), 300 mg (MD = −2.02, 95% CI: −3.12, −0.93, $P < 0.01$), and 1000 mg (MD = −1.00, 95% CI: −2.20, 0.20, $P < 0.01$), which was shown in Figure 3.

Secondary efficacy outcomes

Three secondary efficacy outcomes were assessed, and in comparison, any dose of eptinezumab had a highly significant efficacy, ≥75% migraine responder rate [RR = 1. 80, 95% confidence interval (CI): 1.40, 2.33, $P < 0.001$ Figure 2b], ≥50% migraine responder rate [RR = 1.46, 95% CI: 1.33, 1.61, $P < 0.001$ Figure 2c], and 100% migraine responder rate [RR = 2.41, 95% CI: 1.08, 5.38, $P = 0.03$ Figure 2d]. For migraine responder rate, a subgroup analysis was carried out to compare therapeutic effect at various dosages of eptinezumab, 10 mg (RR = 1.30, 95% CI: 0.82, 2.06, $P = 0.27$ Figure 4a), 30 mg (RR = 1.46, 95% CI: 1.09, 1.95, $P = 0.01$ Figure 4b), 100 mg (RR = 1.59, 95% CI: 1.29, 1.96, $P < 0.01$ Figure 4c), 300 mg (RR = 1.95, 95% CI: 1.60, 2.39, $P < 0.01$ Figure 4d) and 1000 mg (RR = 3.75, 95% CI: 1.63, 7.81, $P < 0.01$ Figure 4e).

Safety outcomes

There was no death among patients included in these four RCTs. Safety of eptinezumab can be demonstrated that no obvious elevation in TEAEs between any dose of eptinezumab and placebo (RR = 1.01, 95% CI 0.94–1.10; $P = 0.71$) [$\chi^2 = 0.28$, $I^2 = 0.0\%$ Figure 5a]. The frequent adverse effects included upper respiratory tract infection (URTI), nasopharyngitis, and nausea as shown in Table 3. In addition, there was no remarkable variation in SAEs at any dose of eptinezumab in comparison to placebo [RR = 0.93, 95% CI 0.46, 1.90; $P = 0.89$) ($\chi^2 = 2.16$, $I^2 = 7\%$ Figure 5b]. The

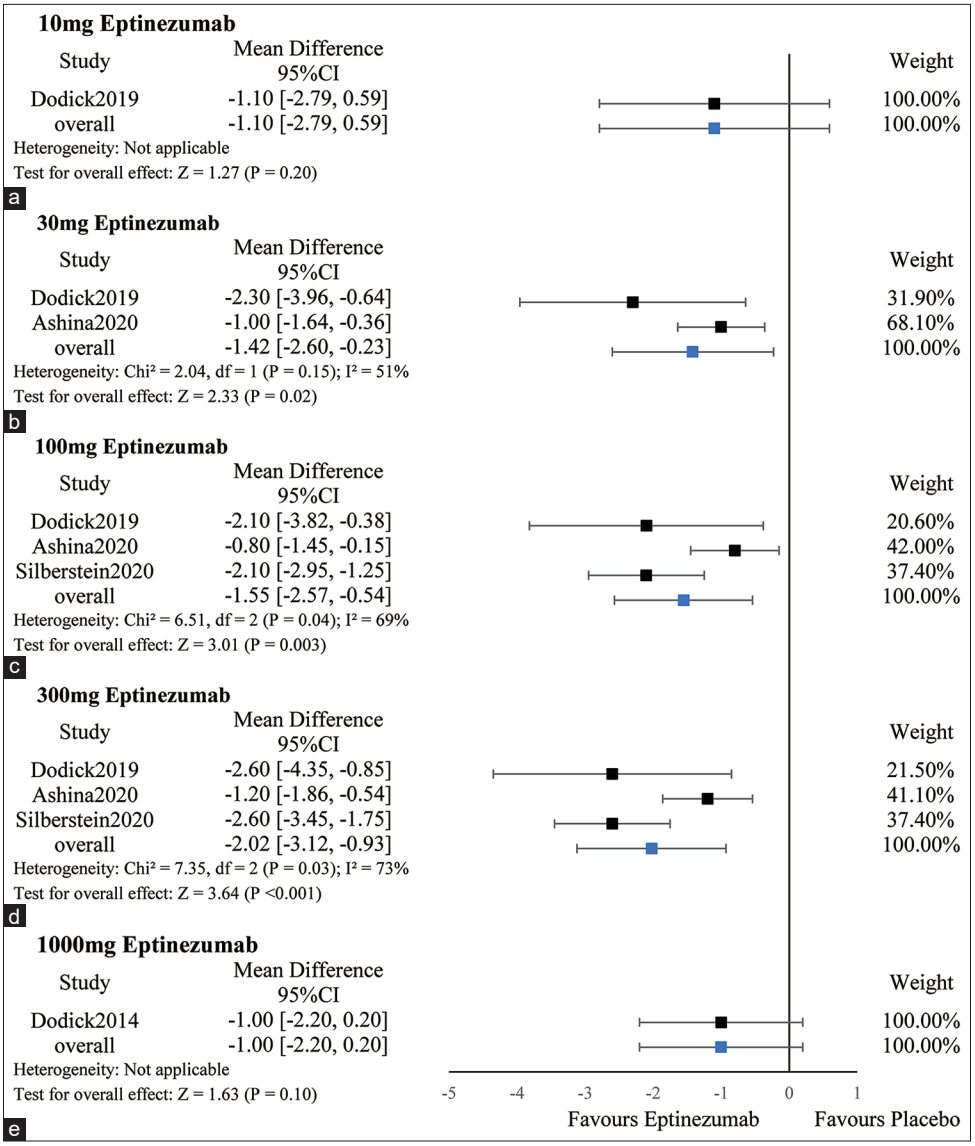

Figure 3: The pooled mean difference (MD) of monthly migraine days (MMDs) in different doses of eptinezumab compared with placebo. Notes: The black squares indicate the estimated MD for each randomized controlled trial (RCT), and the extending lines indicate the estimated 95% confidence interval (CI) of MD for each RCT. Red squares indicate the estimated risk ratio (95% CI) for all patients. Weights are from a random-effects analysis. MD = Mean Difference; CI = Confidence interval; RCT = Randomized controlled trial

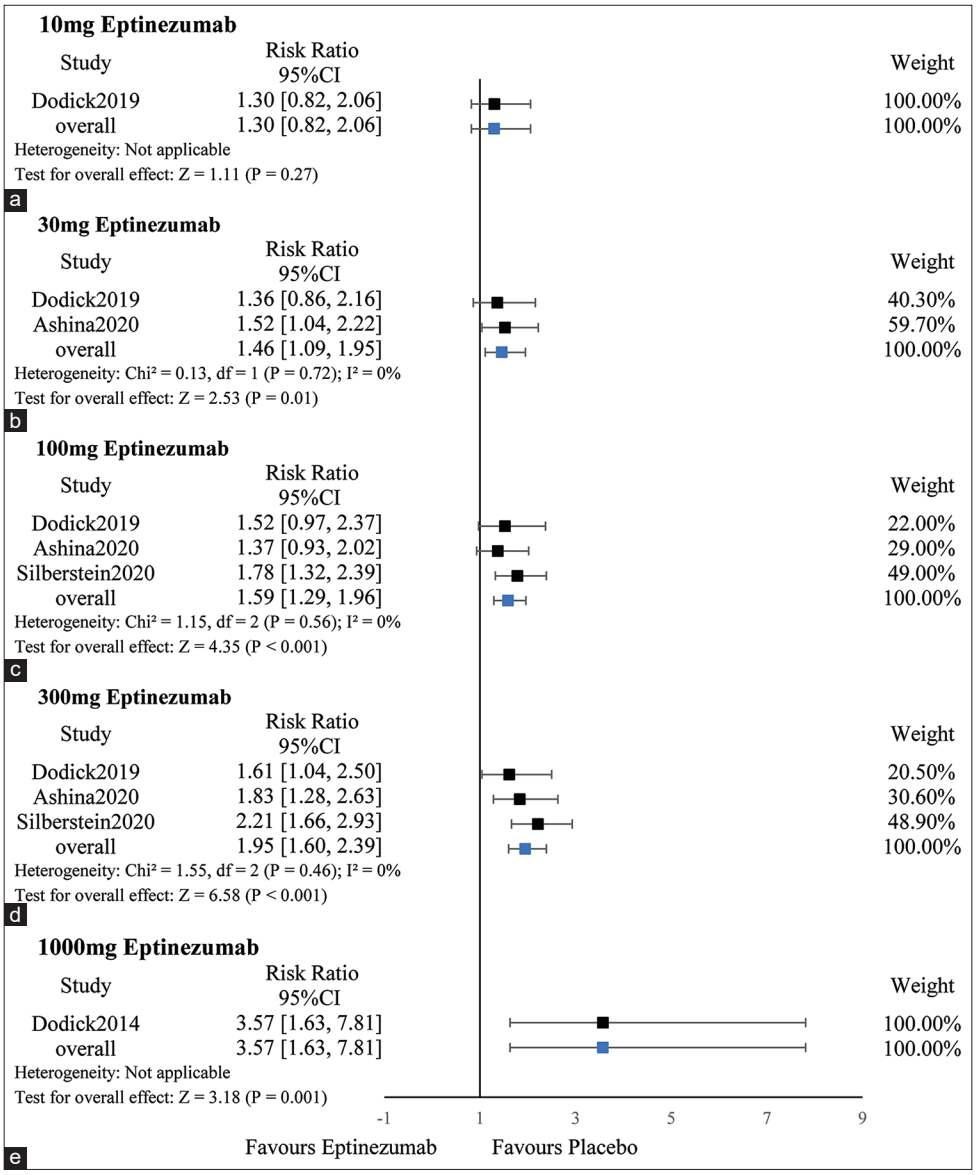

Figure 4: The pooled risk ratio (RR) of 75% migraine responder rate in different doses of eptinezumab compared with placebo. Notes: The black squares indicate the estimated RR for each randomized controlled trial (RCT), and the extending lines indicate the estimated 95% confidence interval (CI) of RR for each RCT. Red squares indicate the estimated RR (95% CI) for all patients. Weights are from a random-effects analysis. RR = Risk Ratio; CI = Confidence interval; RCT = Randomized controlled trial

subgroup analysis of different dosages of eptinezumab was performed in Figure 6 to compare the efficacy difference between these four doses, 10 mg (RR = 1.01, 95% CI: 0.82, 1.26, *P* = 0.91), 30 mg (RR = 0.92, 95% CI: 0.77, 1.10, *P* = 0.35), 100 mg (RR = 1.01, 95% CI: 0.91, 1.11, *P* = 0.92), 300 mg (RR = 1.06, 95% CI: 0.96, 1.17, *P* = 0,24), and 1000 mg (RR = 1.08, 95% CI: 0.82, 1.43, *P* = 0.58).

Risk of bias and sensitivity analyses

The funnel plot [Figure 7] indicated no significant publication bias for the four studies evaluated. Besides, our study conducted a sensitivity test to evaluate whether there was bias in these four included studies. A low risk of selection bias was observed in these included studies. There was an unclear risk of bias for attrition bias and reporting bias in the studies by Ashina and Silberstein, and Dodick's study, in 2014, showed an unclear risk of bias for performance bias and attrition bias, which has been shown in detail in Figure 8. Sensitivity analysis for the four included studies is presented in Figure 9.

DISCUSSION

CGRP has been proven as a crucial role in the development of treatment for migraine.[27] Monoclonal antibodies (mAbs) targeting the CGRP pathway have been demonstrated to be effective in preventing migraine, and were already put into clinical use.[28] Eptinezumab, a novel monoclonal antibody,

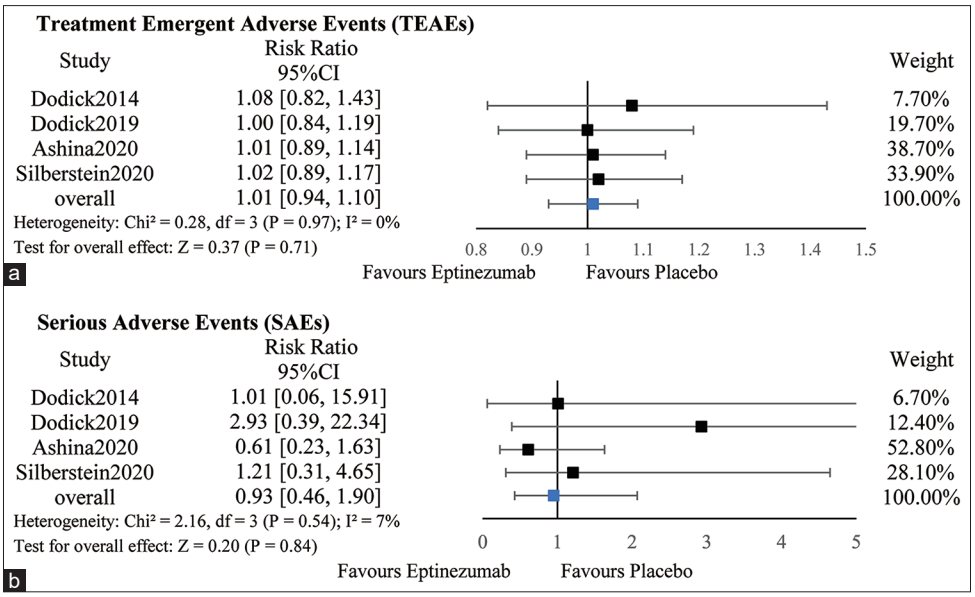

Figure 5: The pooled risk ratio (RR) of safety outcomes of any-dose eptinezumab compared with placebo. Notes: The black squares indicate the estimated RR for each randomized controlled trial (RCT), and the extending lines indicate the estimated 95% confidence interval (CI) of RR for each RCT. Red squares indicate the estimated RR (95% CI) for all patients. Weights are from a random-effects analysis. RR = Risk Ratio; CI = Confidence interval; RCT = Randomized controlled trial

Table 3: Adverse events of eptinezumab versus placebo

Outcome	Number of studies (reference)	Number of events/participants (%)		I^2 (%)	Risk ratio (95% CI)	*P*
		Eptinezumab	Placebo			
Any TEAE	4	1058/1948 (56.7)	414/791 (58.4)	0	1.01 (0.94–1.10)	0.71
Any SAE	4	31/1948 (1.6)	11/791 (1.4)	0	0.93 (0.46–1.90)	0.84
Nausea	4	67/1948 (3.4)	26/791 (3.3)	0	0.92 (0.59–1.44)	0.71
URTI	4	148/1948 (7.6)	48/791 (6.1)	0	1.19 (0.86–1.65)	0.28
Nasopharyngitis	3	123/1867 (6.6)	40/709 (5.6)	0	1.20 (0.85–1.71)	0.30
Migraine	3	28/1282 (2.2)	20/569 (3.5)	13	0.60 (0.29–1.26)	0.18
Dizziness	3	53/1242 (4.3)	18/425 (4.2)	0	0.89 (0.53–1.49)	0.65
Sinusitis	2	49/1161 (4.3)	20/343 (5.8)	9	0.70 (0.41–1.22)	0.21
Bronchitis	2	34/1161 (2.9)	17/343 (5.0)	0	0.56 (0.31–1.02)	0.06
Fatigue	2	24/747 (3.2)	4/304 (1.3)	61	2.43 (0.32–18.27)	0.39
Back pain	2	17/747 (2.3)	11/304 (3.6)	0	0.69 (0.32–1.48)	0.34
Cough	1	15/666 (2.3)	7/222 (3.2)	N/A	0.71 (0.28–1.76)	0.46
Influenza	1	15/666 (2.3)	5/222 (2.3)	N/A	1.00 (0.36–2.78)	1
Diarrhea	1	15/666 (2.3)	3/222 (1.4)	N/A	1.68 (0.48–5.87)	0.41
Tooth abscess	1	3/81 (3.7)	0/82 (0)	N/A	7.09 (0.37–135.03)	0.19
Pyrexia	1	1/81 (1.2)	2/82 (2.4)	N/A	0.51 (0.05–5.47)	0.58
Malaise	1	2/81 (2.4)	0/82 (0)	N/A	5.06 (0.25–103.81)	0.29
Dry mouth	1	3/81 (3.7)	0/82 (0)	N/A	7.09 (0.37–135.03)	0.19
Sciatica	1	2/81 (2.4)	0/82 (0)	N/A	5.06 (0.25–103.81)	0.29
Weight loss	1	2/81 (2.4)	0/82 (0)	N/A	5.06 (0.25–103.81)	0.29
Hyperkalemia	1	2/81 (2.4)	0/82 (0)	N/A	5.06 (0.25–103.81)	0.29
Arthropod bite	1	2/81 (2.4)	0/82 (0)	N/A	5.06 (0.25–103.81)	0.29
Pruritus	1	2/81 (2.4)	0/82 (0)	N/A	5.06 (0.25–103.81)	0.29

TEAE=Treatment-emergent adverse events; SAE=serious adverse event; URTI=Upper respiratory tract infection, N/A=Not applicable; CI=Confidence interval

has already been accepted by the US FDA for the prevention of migraine. However, no previous studies have performed meta-analyses to demonstrate efficacy and safety.

Our study paid attention to the healing effect and safety of eptinezumab. We pooled the primary characteristics of 2739 participants in four RCTs, and we found that the efficacy of eptinezumab was significantly better than placebo, and the safety was virtually indistinguishable from placebo. In addition, this meta-analysis measured the efficacy outcomes of different dosages, which is more instructive for clinical treatment.

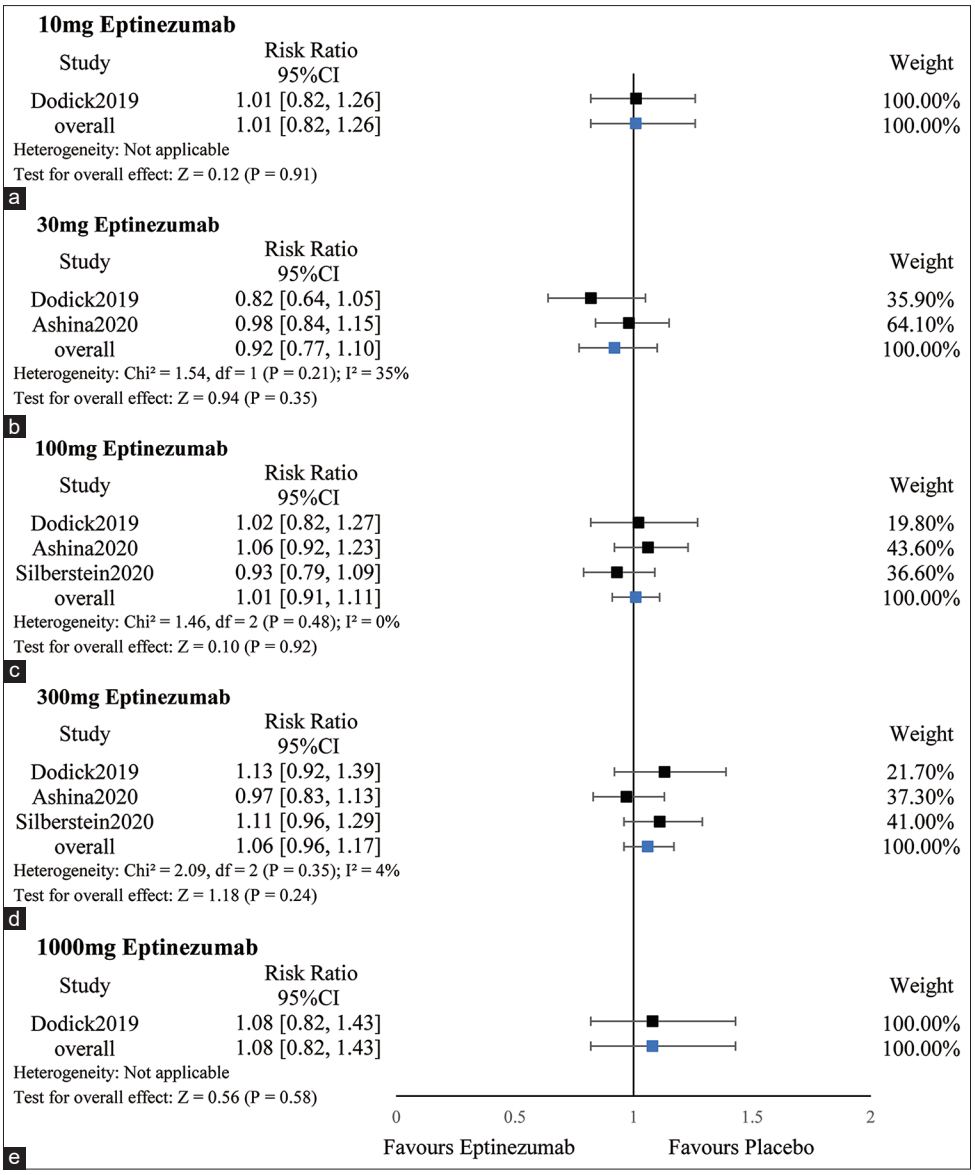

Figure 6: The pooled risk ratio (RR) of treatment-emergent adverse events in different doses of eptinezumab compared with placebo. Notes: The black squares indicate the estimated RR for each randomized controlled trial (RCT), and the extending lines indicate the estimated 95% confidence interval (CI) of RR for each RCT. Red squares indicate the estimated RR (95% CI) for all patients. Weights are from a random-effects analysis. RR = Risk Ratio; CI = Confidence interval; RCT = Randomized controlled trial

In terms of efficacy outcomes, any dose of eptinezumab significantly decreased MMDs compared to placebo (MD = -1.56 $P < 0.001$). In addition, for the three secondary efficacy outcomes, the efficacy of eptinezumab was similarly found. Any dose regimen of eptinezumab improved 75% migraine responder rate (RR = 1.71, $P < 0.001$), the percentage of 50% responder rate (RR = 1.44, $P < 0.001$), and the proportion of 100% responder rate (RR = 2.03, $P < 0.001$).

The other three mAbs (fremanezumab, galcanezumab, erenumab) of the pathway with targeting CGRP were already used for clinical treatment, and their efficacy and safety were reported in three separate meta-analyses. In this meta-analysis, there was a significant improvement of 2.02 days in MMDs with the use of 300 mg eptinezumab compared to the placebo. In the article written by Gao *et al*., the MD in MMDs for fremanezumab versus placebo was 2.21 days.[29] Gklinos and Mitsikostas assessed MMDs of galcanezumab at a dose of 120 mg/day, and the MD was 1.95 days compared to placebo.[30] In the meta-analysis written by Zhu *et al*., the MD was 1.32 days.[31] Although no direct comparison could not be made, it was all in comparison with a placebo; hence, we consider that fremanezumab had better efficacy than other mAbs with the same target in the treatment of migraine, followed by eptinezumab, galcanezumab, and erenumab.

Our research found no statistically remarkable difference (RR = 1.01, $P = 0.83$) in the primary safety outcome TEAE between eptinezumab and placebo. Although minor adverse reactions have occurred, such as URTI ($P = 0.30$),

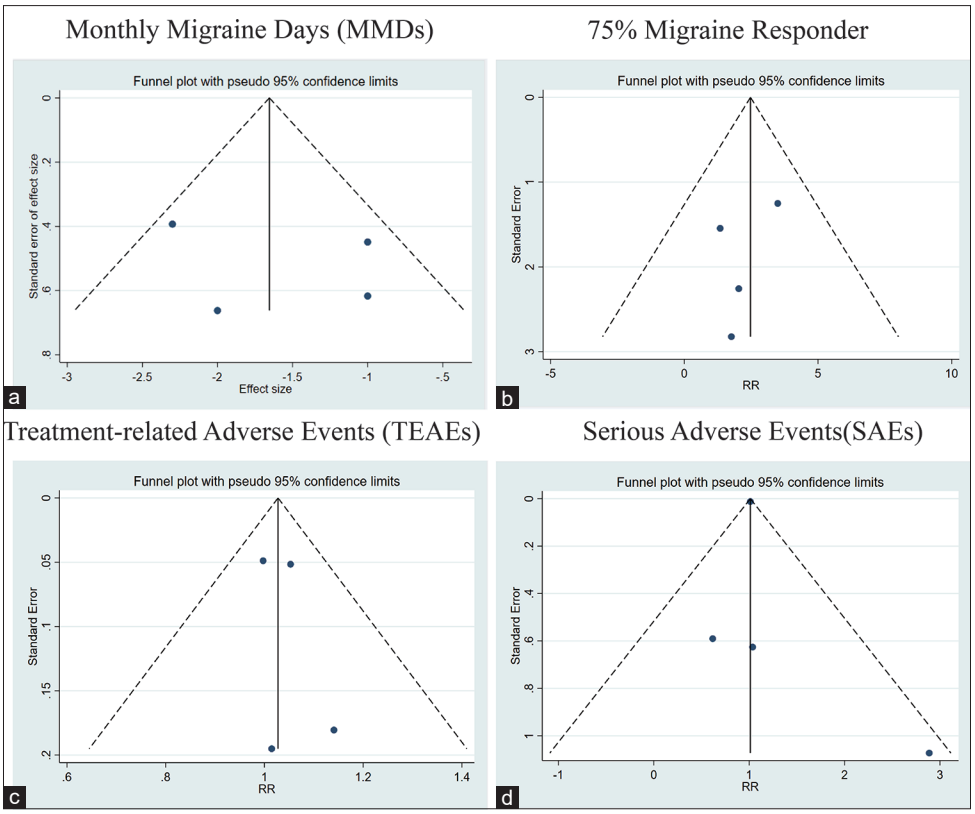

Figure 7: The funnel plots of included studies. Symmetrical distributions of studies were presented regarding four different outcomes, including (a) monthly migraine days, (b) 75% migraine responder rate, (c) treatment-emergent adverse events, and (d) serious adverse events

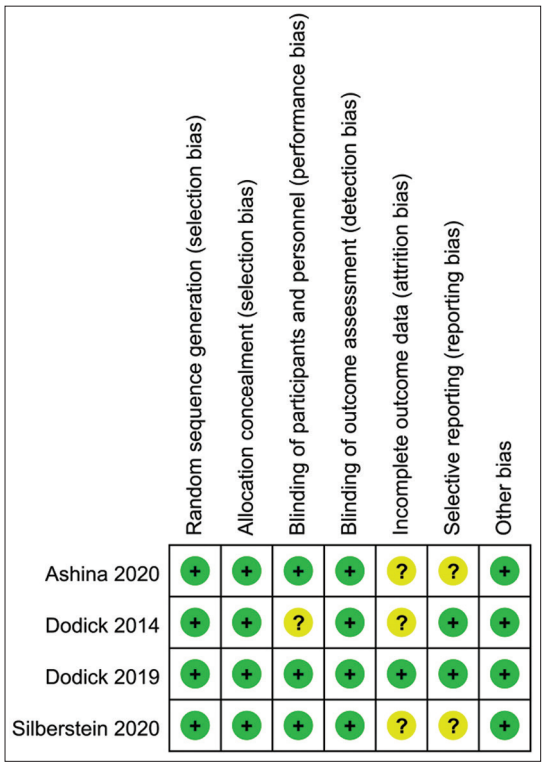

Figure 8: Risk of bias: a summary table for each risk of bias item for each study

nasopharyngitis (P = 0.30), and nausea (P = 0.62), we believe that eptinezumab is well tolerated. In addition, in regard to the occurrence of SAEs, eptinezumab caused few serious adverse reactions. In conclusion, we believe that the safety of eptinezumab for migraine can be guaranteed. The meta-analysis authored by Gao *et al*. revealed that the patients treated with fremanezumab were 1.21 times (P < 0.01) more likely to experience TEAE than the placebo.[29] In the meta-analysis written by Gklinos and Mitsikostas, RR in TEAE for galcanezumab versus placebo was 1.12 (P < 0.01).[30] A meta-analysis by Zhu *et al*.[31] concluded a good safety profile for the treatment of erenumab (RR = 0.97, P = 0.49). Although direct comparisons could not be made, we considered that eptinezumab and erenumab had better tolerance than the other two antibodies.

In a subgroup analysis of the different doses of eptinezumab, the dosages of 30 mg, 100 mg, 300 mg, and 1000 mg all had good efficacy versus placebo, particularly 300 mg. For 30 mg and 100 mg eptinezumab, we found no obvious difference in efficacy outcomes between these two dosages. However, eptinezumab at the dose of 300 mg had a more pronounced reduction in MMDs than the other four different doses of eptinezumab, and similar for the secondary efficacy. In addition, our analysis consisted subgroup analyses of safety according to different doses, and finally, no statistically significant difference occurred among these four different doses of eptinezumab compared with placebo; hence, we did not believe that the incidence

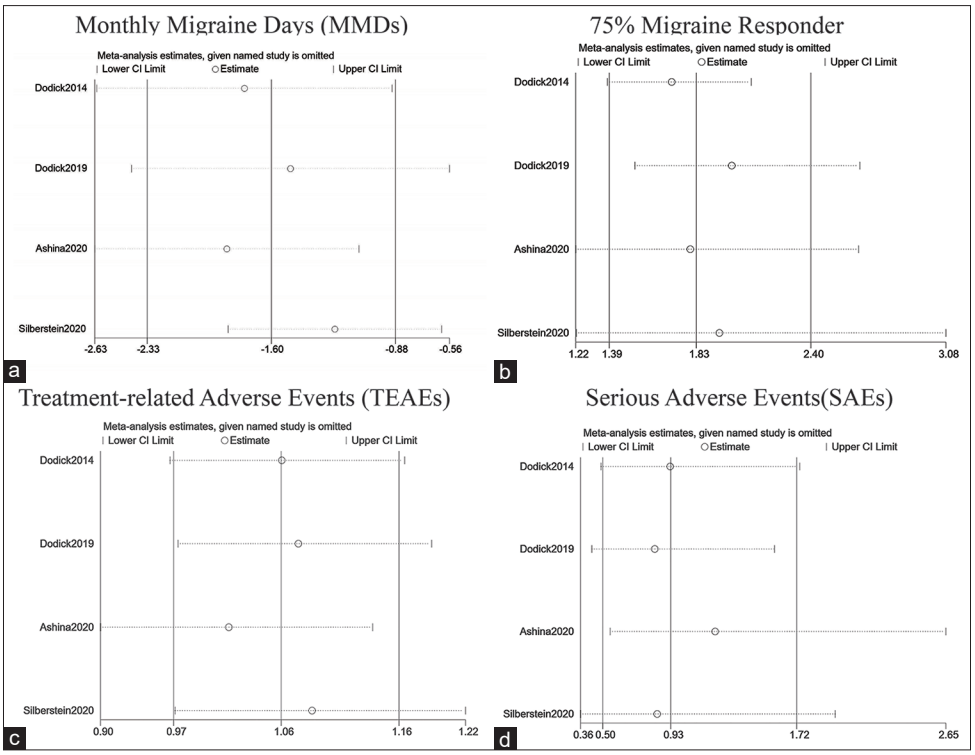

Figure 9: The result of sensitivity analysis. Sensitivity analyses were conducted for the following four different outcomes, including (a) monthly migraine days, (b) 75% migraine responder rate, (c) treatment-emergent adverse events, and (d) serious adverse events

of adverse events increases with an additional dose. As only one of the included studies[21] mentioned the 10 mg dose of eptinezumab and only one study[24] mentioned the 1000 mg dose of eptinezumab, we lack sufficient data to demonstrate the therapeutic efficacy and safety of the dosage of 10 and 1000 mg compared with other doses; therefore, we do not recommend 10mg and 1000 mg as the usual dose of eptinezumab, although they are both efficacious in treating migraine in this study. We also noticed one study from 2021[32] that mentioned the curative effect and security of 100 mg of eptinezumab compared with placebo. This study concluded that compared to placebo, the time of headache and symptom relief was shortened by intravenous eptinezumab. However, this study focused on short-term (within 24 h) efficacy and safety, meanwhile using a different dosing method (intravenous); hence, we did not include this study; however, it demonstrates the efficacy and safety of this drug as well. Meanwhile, we expect more different doses of eptinezumab to be put into clinical trials and more clinical data to prove the *curative effect* and safety of eptinezumab.

Several limitations are objectively included in this study. First, the sample size was limited, only four RCTs were included in this article, and the number of participants contained in the studies was not large enough to obtain more significant differences. This analysis lacked sufficient data to analyze the *curative effect* and safety of the dosage of 10 mg, and it is hoped that more clinical data will be available to verify this. Furthermore, it is not clear whether there are other measures of the drug used to treat migraine. Second, there is a lack of long-term management as all efficacy and safety outcomes were only available after 12 weeks of drug administration, and follow-up visits were not included. In addition, these studies only analyzed and documented eptinezumab at different doses for weeks 1–12, without mentioning the efficacy and adverse events arising from the subsequent continuation of eptinezumab.

CONCLUSION

Eptinezumab demonstrates excellent efficacy and low adverse events in treating migraine, shortening MMDs, and reducing migraine responder rate risk, but with little adverse events. Further, eptinezumab at the dose of 300 mg had more significant efficacy outcomes. Finally, we hope that more large-scale clinical trials will be completed to prove the safety and efficacy of eptinezumab.

Data availability

Data availability is not applicable to this article as no new data were created or analyzed in this study.

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Yi Zhong and Jiahe Wang made significant contributions to the study concept and design, data collection, analysis and interpretation of data, and drafting of the research; Hang Li and Siyuan Yang supervised the data analysis and

made strict revisions to the critical intellectual content of the article; Xiang Li, Heng Gao, and Gang Chen participated in the design of the article and revised the article. This version of the article has received finally by final permission for submissions from all authors.

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Conflicts of interest

The authors declared that they had no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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