Systematic Review and Meta-Analysis

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Dexamethasone-sparing regimen is an effective and safe alternative in overall antiemetic protection

A systematic review and meta-analysis

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Abstract

Objective: We performed a meta-analyisis to evaluate the efficacy of maintenance dexamethasone against acute or delayed chemotherapy-induced nausea and vomiting (CINV) in patients receiving moderately or highly emetic risk chemotherapy regimen.

Methods: PubMed, Embase, and Cochrane Library were searched for eligible studies. Data comparing maintenance dexamethasone with single-dose dexamethasone during the acute, delayed, and overall phase of CINV were extracted. Overall risk ratio (RR) was used to estimate the efficacy and adverse effects.

Results: Nine studies were included. In delayed phase, maintenance dexamethasone has similar efficacy to single-dose dexamethasone for no emetic episodes (RR, 1.06; 95% confidence interval [CI], 1.00–1.14), complete response (RR, 1.04; 95% CI, 0.98–1.11), complete control (RR, 1.07; 95% CI, 0.98–1.16), and total control (RR, 1.06; 95% CI, 0.91–1.23). In overall phase, maintenance dexamethasone has similar efficacy to single-dose dexamethasone for no emetic episodes (RR, 1.02; 95% CI, 0.94–1.11), complete response (RR, 1.02; 95% CI, 0.95 -1.09), complete control (RR, 1.03; 95% CI, 0.94–1.13), total control (RR, 1.05; 95% CI, 0.90–1.23), and no rescue medication (RR, 1.07; 95% CI, 0.97–1.19). Maintenance dexamethasone was only superior to single-dose dexamethasone for no rescue medication during delayed phase (RR, 1.10; 95% CI, 1.01–1.21, $P = .034$). The incidence of hiccup was observed higher in maintenance dexamethasone group (RR = 3.16, 95% CI, 1.12–8.92).

Conclusion: The single-dose dexamethasone regimen offers high and similar overall control of symptoms as the maintenance dexamethasone regimen in this population. Multiple-day dexamethasone was suitable for patients who used rescue medication during the delayed phase.

Abbreviations: AC = anthracycline/cyclophosphamide, CC = complete control, CINV = chemotherapy-induced nausea and vomiting, CR = complete response, HEC = highly emetogenic chemotherapy, MEC = moderately emetogenic chemotherapy, MeSH terms = medical subject heading terms, NCCN = National Comprehensive Cancer Network, OR = odds ratio, RR = risk ratio, TC = total control.

Keywords: anti-emetic, cancer, chemotherapy, dexamethasone

1. Introduction

Chemotherapy-induced nausea and vomiting (CINV) has a deleterious influence on the performance status and health-related quality of life of patients receiving chemotherapy.[1] CINV consists of 2 phases: acute-phase CINV occurs within 24 hours of the initial chemotherapy administration, whereas delayed-phase

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CINV can last for up to 120 hours after chemotherapy administration.[2] The mechanisms and pharmacophysiological pathways are different between acute and delayed phase of CINV[3,4]; hence, distinct medication strategies are maneuvered. In a study of 1910 patients receiving highly emetogenic chemotherapy (HEC) or moderately emetogenic chemotherapy (MEC), Tamura et al reported that acute nausea of CINV could be well processed (20.8% with HEC and 6.7% with MEC). However, half of the patients reported suffering from delayed nausea (49.4% with HEC and 41.7% with MEC).[5] CINV in delayed phase remains a crucial challenge in tumor treatment.

Despite the advance in supportive care that occurred with the introduction of the first-generation serotonin (5-HT3)-receptor antagonists (eg, granisetron, ondansetron, and dolasetron), up to 70% of patients with tumor receiving HEC agents suffered from nausea and vomiting after chemotherapy.[6] Palonosetron, a newer second-generation 5-HT3, has a longer half-time (about 40 hours) and a higher binding affinity to 5-HT3 receptors than first generation of 5-HT3 antagonists.[7] Palonosetron is demonstrated to be more efficient and beneficial than first generation of 5-HT3 antagonists against delayed emesis.[8] Dexamethasone is effective against CINV, combined with a 5-HT3 antagonist. For high emetic risk regimens, triple antiemetic therapy using aprepitant (a NK-1 receptor antagonist), 5-HT3 antagonist, and dexamethasone is recommended.[9]

Dexamethasone was recommended for several days to control CINV associated with HEC and MEC by current guideline of NCCN (http://www.nccn.org). However, Ito et al[10] reported that dexamethasone on days 2 and 3 could be spared when combined with NK-1 receptor antagonist and palonosetron in HEC. In several studies, researchers compared the efficacy of maintenance dexamethasone regimen to single-dose dexamethasone regimen. The present analysis was conducted to enhance evidence for the comparison of maintenance dexamethasone regimen and single-dose dexamethasone regimen.

2. Methods

2.1. Search strategy

We systematically searched the literature on PubMed, Embase, and Cochrane Library (from the beginning of 1992 to February, 2018). The search strategy was based on "dexamethasone," "chemotherapy," AND "vomit OR emesis" as keywords or MeSH terms (medical subject heading terms). All titles and abstracts were screened to select eligible articles independently by 2 reviewers (Y-LG and JR). Trials not published in English were excluded in present analysis. Each eligible study must meet the following criteria: studies to compare the efficacy of maintenance dexamethasone versus single-dose dexamethasone; maintenance dexamethasone and single-dose dexamethasone used for CINV; and sufficient variables for figuring risk ratio (RR) of complete response (CR). When studies had overlapping cohorts, we only included the one with largest number of participants.

2.2. Definition of outcomes

The primary endpoint was the prop risk ration of patients achieving a CR. CR was defined as no rescue medication and no emetic episodes. Secondary endpoints included the percentage of patients achieving either a complete control (CC: no emetic episodes, no rescue medication, and no significant nausea), total control (TC: no emetic episodes, no rescue medication, and no nausea), taking no rescue medications or no emesis during the acute, delayed, and overall phase.

2.3. Data extraction

Two reviewers (Y-LG and J-MX) extracted the data from total potential studies independently. The following information from each included studies was captured: first author's name, publication year, mean age, emetogenicity, the detailed treatment regimens, the number of patients in maintenance dexamethasone group, and single-dose dexamethasone group and antiemetic response.

2.4. Quality assessment

The quality of eligible trials was assessed by 2 reviewers (Y-LG and JR) according to Cochrane Collaboration Reviewers' Handbook for Systematic Reviews of Interventions. Sequence generation, allocation concealment, blinding, incomplete outcome data, and selective outcome reporting were evaluated independently. The quality assessment of eligible studies is described in Table 1.

2.5. Statistical analysis

Pooled estimates of odds ratio (OR) were chosen, whereas the events rate was <1%.[11] Otherwise, pooled estimates of RR were selected. A heterogeneity test was examined using Q statistics.[12] When heterogeneity was negative, which was defined as I^2 <50%, fixed-effects model[13] was utilized; otherwise, the

Table 1

Quality assessment of included studies.

Study	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	No selective outcome reporting	Other sources of bias
Celio et al[17]	Low risk	Low risk	High risk	Low risk	Unclear	Low risk
Aapro et al[16]	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear
Furukawa et al[18]	Low risk	Low risk	Unclear	Low risk	Unclear	Unclear
Matsuura et al[19]	Low risk	Low risk	Unclear	Low risk	Unclear	Unclear
Kosaka et al[20]	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear
Komatsu et al[8]	Low risk	Low risk	High risk	Low risk	Unclear	Low risk
Inoue et al[15]	Low risk	Low risk	Unclear	Low risk	Unclear	Low risk
Sasaki et al[21]	Low risk	Unclear	Unclear	Unclear	Unclear	Unclear
Ito et al[10]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

random-effects model[14] was utilized. Egger linear regression and funnel plot were used to measure potential publication bias. If the *P* value of Egger linear regression was <0.05 or the funnel plot was asymmetrical, it indicated that publication bias may exist. All analyses in this study were processed with the program Stata, version 13.0 (StataCorp LP).

2.6. Subgroup analysis

The primary subgroup analysis was conducted to evaluate the differences between chemotherapy emetogenicities and risk levels. We sorted studies according to chemotherapy emetogenicities. All participants included in this analysis were classified as moderate risk or high risk according to the antiemesis guidelines of the National Comprehensive Cancer Network (NCCN, http://www.nccn.org). We conducted a second subgroup analysis by classifying studies based on antiemetic regimens, age categories, and sex.

2.7. Ethics statement

This article is a secondary data processing of previously published studies. No human or animal experiments were conducted. Ethical approval was not necessary.

3. Results

3.1. Eligible trials

Nine studies,[8,10,15–21] with 1968 cases were included in our meta-analysis (The flowchart was presented in PRISMA Flow Diagram). Three trials[22–24] were excluded because of repetitive data. Considering the heterogeneity and progress of chemotherapy and treatment options, 1 trial[25] was excluded. Among the 1968 patients, 981 patients were treated with maintenance dexamethasone and 987 patients were treated with single-dose dexamethasone. The characteristics of included trials were listed in Table 2.

3.2. Pooled efficacy of maintenance dexamethasone versus single-dose dexamethasone

3.2.1. Efficacy—acute phase. Because both groups are treated with the same antiemetic regimens within the initial 24 hours, the efficacy of antiemetic regimens was not significantly different during the acute phase (Fig. 1).

No emetic episodes were seen. Only 2 studies reported vomiting incidence. Forty-four of 330 cases in maintenance dexamethasone group and 40 of 314 cases in single-dose dexamethasone group suffer from vomiting. Overall RR for no

Table 2

Summary of the main characteristics of all eligible studies.

Study	Year	Interventions on day 1	Interventions on day 2 and 3	Emetogenicity	Percentage female	Mean age, y	Country
Celio et al[17]	2011	Palonosetron 0.25 mg i.v. and Dex 8 mg i.v.	Dex 8 mg p.o. daily on days 2 and 3	MEC	65%	57.0	Italy
Aapro	2010	Palonosetron 0.25 mg i.v. and Dex 8 mg i.v.	Dex 4 mg p.o. b.i.d daily on days 2 and 3	MEC	100	52.1	Austria, Germany, Italy, and Spain
Furukawa et al[18]	2015	Palonosetron 0.75 mg i.v. and Dex 20 mg i.v.	Dex 8 mg p.o. daily on days 2 and 3	HEC	100	60.4	Japan
Matsuura et al[19]	2015	Palonosetron 0.75 mg i.v. and Dex 9.9 mg i.v.	Dex 8 mg p.o. daily on days 2 and 3	HEC	100	57.2	Japan
Kosaka al[20]	2016	Palonosetron 0.75 mg i.v., Dex 9.9 mg i.v. and aprepitant 125 mg p.o.	Dex 8 mg i.v. and aprepitant 80 mg daily on days 2 and 3	HEC	100	53.3	Japan
Komatsu et al[8]	2015	Palonosetron 0.75 mg i.v. and Dex 9.9 mg i.v.	Dex 8 mg p.o. or 6.6 mg i.v. daily on days 2 and 3	MEC	43	64.0	Japan
Inoue et al[15]	2003	Granisetron 3 mg i.v. and Dex 8 mg i.v.	Dex 8 mg i.v. daily on days 2–4	MEC	34	59.0	Japan
Sasaki et al[21]	2013	Palonosetron 0.75 mg i.v., Dex 9.9 mg i.v.	Dex 8 mg i.v. or p.o. daily on days 2–3	MEC	NR	NR	NR
Ito et al[10]	2018	Palonosetron 0.75 mg i.v., Dex 12 mg i.v. and aprepitant 125 mg p.o. or fosaprepitant 150 mg i.v.	Dex 8 mg i.v. or p.o. and aprepitant 80 mg daily on days 2 and 3	HEC	80	54.5	NR

HEC = highly emetogenic chemotherapy, MEC = moderately emetogenic chemotherapy, NR = not report.

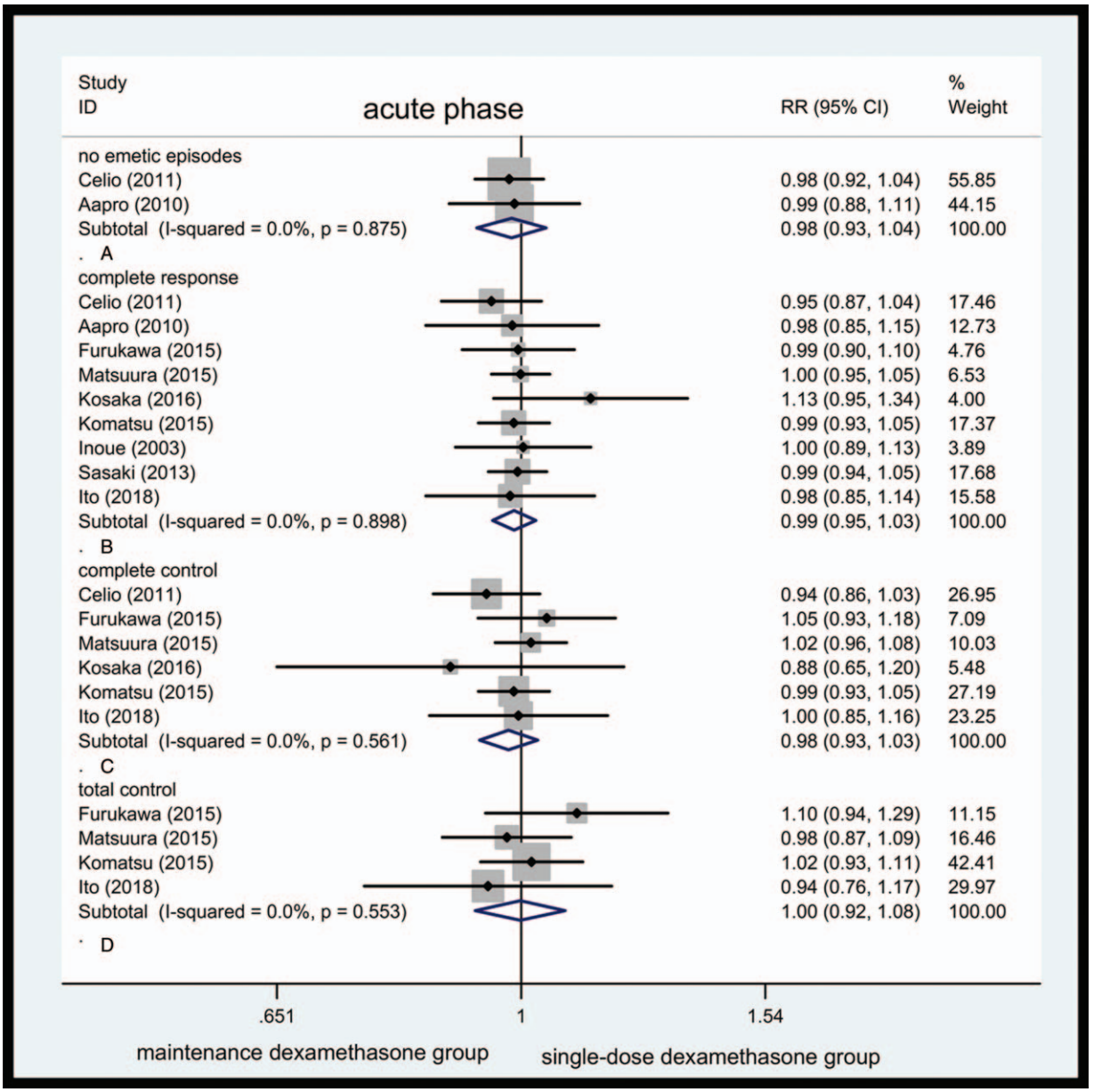

Figure 1. Forest plot showing pooled results for maintenance dexamethasone versus single-dose dexamethasone in acute phase. Pooled risk ratio for no emetic episodes (A). Pooled risk ratio for complete response (B). Pooled risk ratio for complete control (C). Pooled risk ratio for total control (D).

emetic episodes was 0.98 (95% CI, 0.93–1.04, Fig. 1A). It failed to achieve a statistical significance. The heterogeneity was not observed; the fixed-effects model was preferred (Table 1).

- CR: 9 studies reported CR in 808 of 981 cases in maintenance dexamethasone group and 822 in 987 cases in single-dose dexamethasone group. The overall RR for CR was 0.99 (95% CI, 0.95–1.03, Fig. 1B). The heterogeneity of CR for this comparison was not observed.
- CC: 6 studies documented CC in 509 of 644 cases in maintenance dexamethasone group and 527 of 651 cases in single-dose dexamethasone group. Pooled RR for CC was 0.98 (95% CI, 0.93–1.03, Fig. 1C).
- TC: Only 4 studies were available for this variable. Three-hundred four of 442 cases in maintenance dexamethasone and 310 of 450 cases in single-dose dexamethasone group showed TC. The RR for TC was 1.00 (95% CI, 0.92–1.08, Fig. 1D).

No rescue medication was taken. No article recorded this variable; thus, no calculations could be made.

3.2.2. Efficacy—delayed phase. Values between 24 and 120 hours after initial chemotherapy were pooled and forest plot was listed in Figure 2.

No emetic episodes were seen. Only 2 studies reported vomiting incidence, with pooled RR of no emetic episodes being 1.06 (95% CI, 1.00–1.14, Fig. 2A); no statistical differences were observed in this outcome ($P = .065$). A total of 272 of 310 cases in maintenance dexamethasone group and 259 of 314 cases in single-dose dexamethasone group reported no emetic episodes. The heterogeneity was not observed in this comparison.

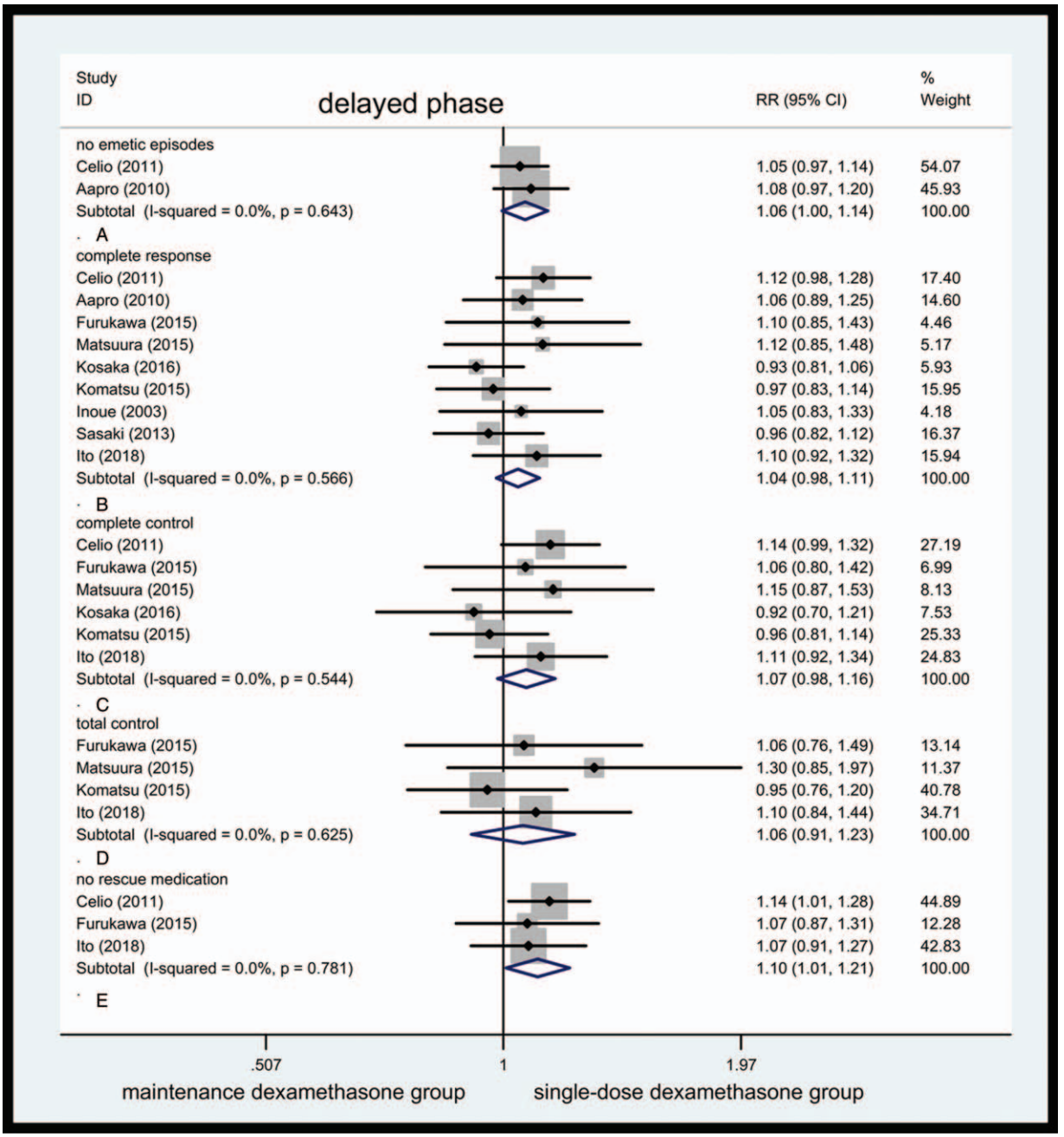

Figure 2. Forest plot showing pooled results for maintenance dexamethasone versus single-dose dexamethasone in delayed phase. Pooled risk ratio for no emetic episodes (A). Pooled risk ratio for complete response (B). Pooled risk ratio for complete control (C). Pooled risk ratio for total control (D). Pooled risk ratio for no rescue medication (E).

- CR: 9 clinical trials enclosed these variables. Nine studies reported CR in 665 of 981 cases and 641 of 987 cases in maintenance dexamethasone group and single-dose dexamethasone group. The pooled RR for CR was 1.04 (95% CI, 0.98–1.11, Fig. 2B).
- CC: 6 studies reported CR in 419 of 644 cases in maintenance dexamethasone group and 397 of 652 cases in single-dose dexamethasone group. The pooled RR for CC was 1.07 (95% CI, 0.98–1.16, Fig. 2C).
- TC: Only 4 studies were available for this variable. A total of 197 of 442 cases in maintenance dexamethasone and 190 of 450 cases in single-dose dexamethasone group showed TC. The pooled RR for TC was 1.06 (95% CI, 0.91–1.23, Fig. 2D).

No rescue medication was taken. Three enrolled studies documented this values, sum of 2 groups had 802 cases. A total of 287 patients in maintenance dexamethasone group and 267 in single-dose dexamethasone group did not require rescue medication. Above this comparison, heterogeneity was not observed, with RR being 1.10 (95% CI, 1.01–1.21, Fig. 2E). The pooled RR for no rescue medication was statistically different ($P = .034$) despite only 3 trials reporting this variable.

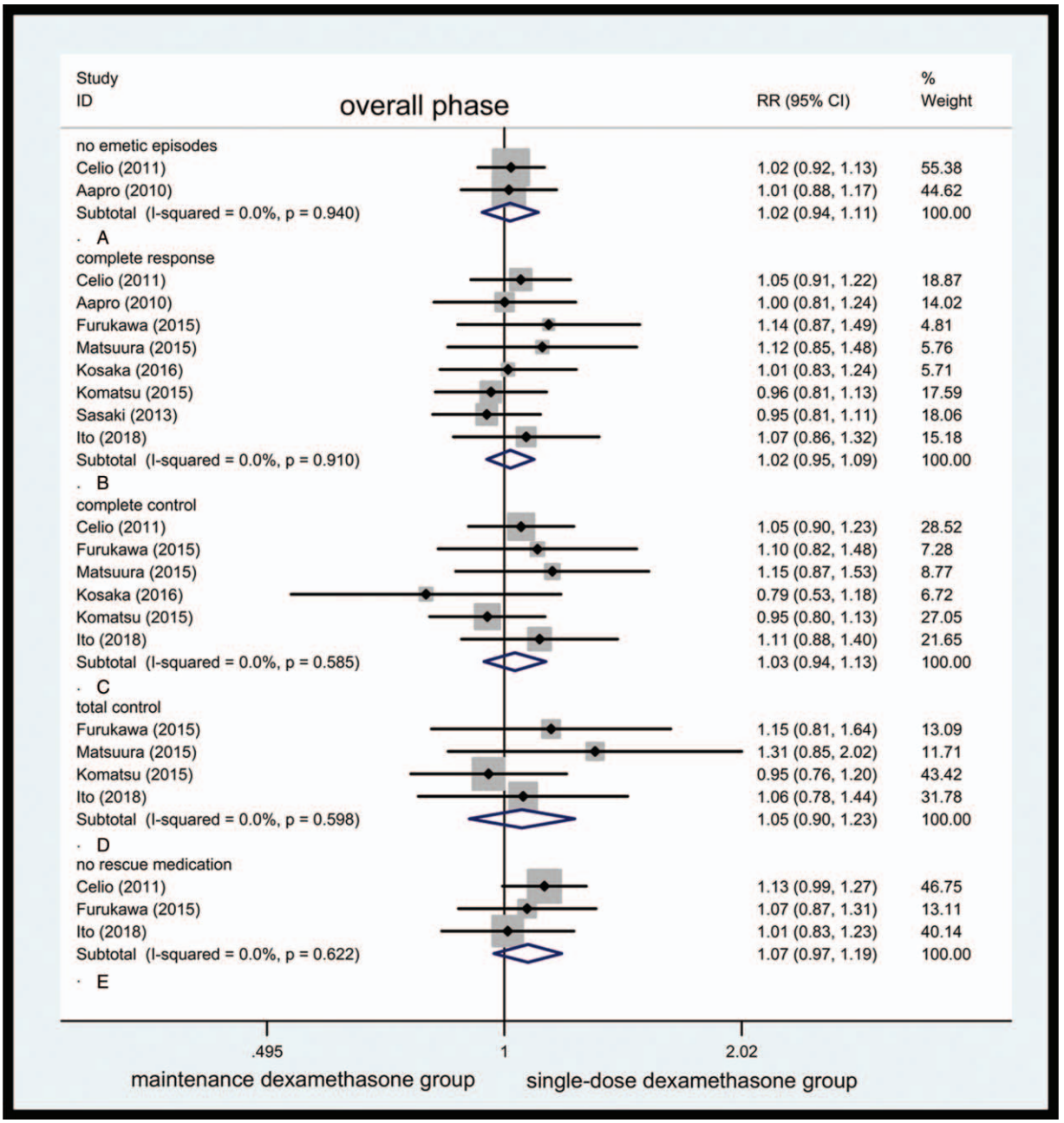

Figure 3. Forest plot showing pooled results for maintenance dexamethasone versus single-dose dexamethasone in overall phase. Pooled risk ratio for incidence of no emetic episodes (A). Pooled risk ratio for complete response (B). Pooled risk ratio for complete control (C). Pooled risk ratio for total control (D). Pooled risk ratio for no rescue medication (E).

3.2.3. Efficacy—overall phase. Variables for the total period were pooled and forest plot was listed in Figure 3.

No emetic episodes were seen. Two studies reported vomiting incidence, where 243 of 310 cases did not vomit in maintenance dexamethasone group and 242 of 314 cases did not vomit in single-dose dexamethasone group at least once during the above duration. The pooled RR for no emetic episodes was 1.02 (95% CI, 0.94–1.11, Fig. 3A). The heterogeneity for the above comparison was of nonexistence.

- CR: 8 clinical trials reported the desired variables. A total of 582 of 946 cases in maintenance dexamethasone group and 576 of 954 cases in single-dose dexamethasone group showed CR. The pooled RR for CR was 1.02 (95% CI, 0.95–1.09, Fig. 3B).
- CC: 6 clinical trials reported the CC 375 of 644 patients in maintenance dexamethasone group and 368 of 652 patients in single-dose dexamethasone group reported CC. The RR for CC was 1.03 (95% CI, 0.94–1.13, Fig. 3C). The heterogeneity was not observed in this comparison.
- TC: Only 4 studies were available for this variable. One hundred eighty-two of 442 cases in maintenance dexamethasone and 176 of 450 cases in single-dose dexamethasone group behaved TC. The RR for TC was 1.05 (95% CI, 0.90–1.23, Fig. 3D).

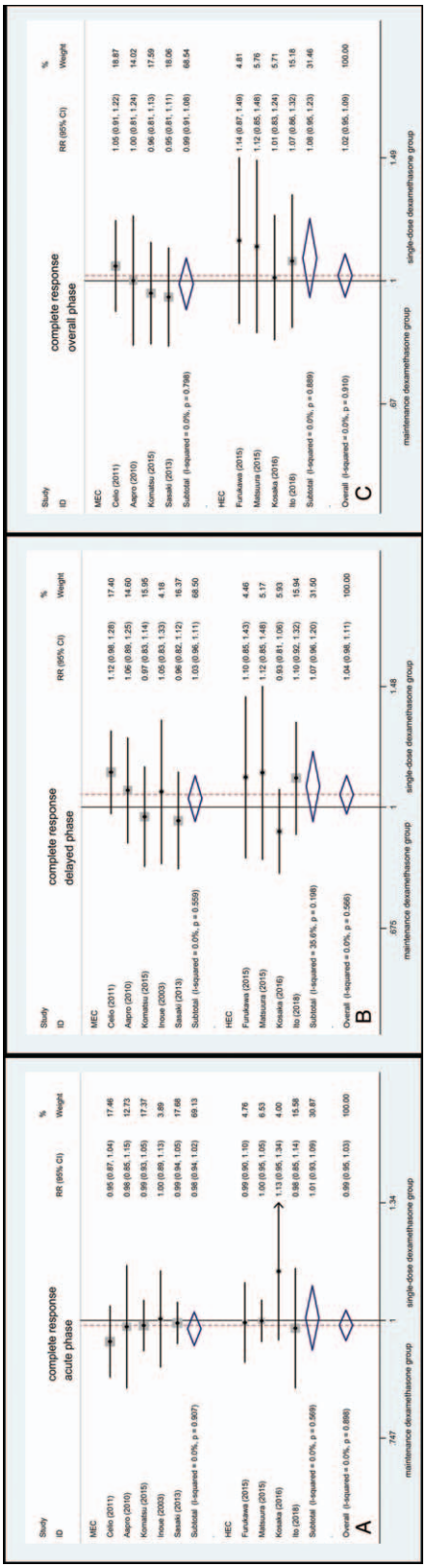

Figure 4. Forest plot for complete response of subgroup analysis of the emetogenic potential.

No rescue medication was taken. Two hundred sixty-oneof 396 patients in maintenance dexamethasone group and 250 of 406 patients in single-dose dexamethasone group did not require additional rescue antiemetic, with RR being 1.07 (95% CI, 0.97–1.19, Fig. 3E).

3.3. Subgroup analyses

Among subgroup emetogenicity analysis, maintenance dexamethasone has similar efficacy to single-dose dexamethasone in both HEC and MEC group during the acute (Fig. 4A), delayed (Fig. 4B), and overall phase (Fig. 4C). The RR for CR in MEC was 0.98 (95% CI 0.94–1.02, Fig. 4A) and the RR for CR in HEC was 1.01 (95% CI, 0.93–1.09, Fig. 4A) in acute phase. The RR for CR in MEC was 1.03 (95% CI, 0.96–1.11, Fig. 4B) and the RR for CR in HEC was 1.07 (95% CI 0.96–1.20, Fig. 4B) in delayed phase. The RR for CR in MEC was 0.99 (95% CI, 0.91–1.08, Fig. 4C) and the RR for CR in HEC was 1.08 (95% CI, 0.95–1.23, Fig. 4C) in overall phase.

Among subgroup antiemetic regimens analysis, statistical significance favoring maintenance dexamethasone was not found during the acute (Fig. 5A), delayed (Fig. 5B), and overall phase (Fig. 5C). The RR for CR in palonosetron group was 1.01 (95% CI, 0.93–1.09, Fig. 5C) in overall phase. The RR for CR in aprepitant group was 1.05 (95% CI, 0.89–1.24, Fig. 5C) in overall phase.

Upon the subgroup analysis of age categories or sex, CR rates showed no difference between treatment groups (Fig. 6).

3.4. Adverse effects

The common adverse effects reported among the included studies were constipation, diarrhea, headache, abdominal pain, hiccup, insomnia, anorexia, erythema, and fatigue. The incidence of hiccup was observed higher in maintenance dexamethasone group (RR = 3.16; 95% CI, 1.12–8.92). These data were only reported in 2 studies. The incidence of diarrhea (RR = 1.38; 95% CI, 0.28–6.64), abdominal pain (RR = 1.27; 95% CI, 0.50–3.24), erythema (RR = 1.13; 95% CI, 0.46–2.78), fatigue (RR = 0.55; 95% CI, 0.24–1.23), constipation (RR = 0.92; 95% CI, 0.63–1.34), headache (RR = 0.89; 95% CI, 0.63–1.25), insomnia (RR = 1.55; 95% CI, 0.77–3.09), and anorexia (RR = 1.17; 95% CI, 0.64–2.14) showed statistical similarity.

3.5. Assessment of publication bias

No emetic episodes were seen. The sample size was too small to perform Egger regression test (only 2 studies were included).

- CR: The funnel plot was subjective to evaluate publication bias (Fig. 7A). No publication bias was observed in Egger linear regression because the intercept of Egger regression test was reported at 1.34202 and *P* value was .302 (Fig. 7B).
- CC: Publication bias was not attained in this analysis. The intercept was reported at −0.7597613 with a *P* value of .633 (Fig. 7C).
- TC: No publication bias could be achieved in this comparison. The intercept was reported at 2.96113 (*P* = .110, Fig. 7D).

No rescue medication was taken. Egger regression test was not available owing to the insufficient data.

4. Discussion

John et al showed that dexamethasone offered an obvious superiority against emesis among both the acute and delayed

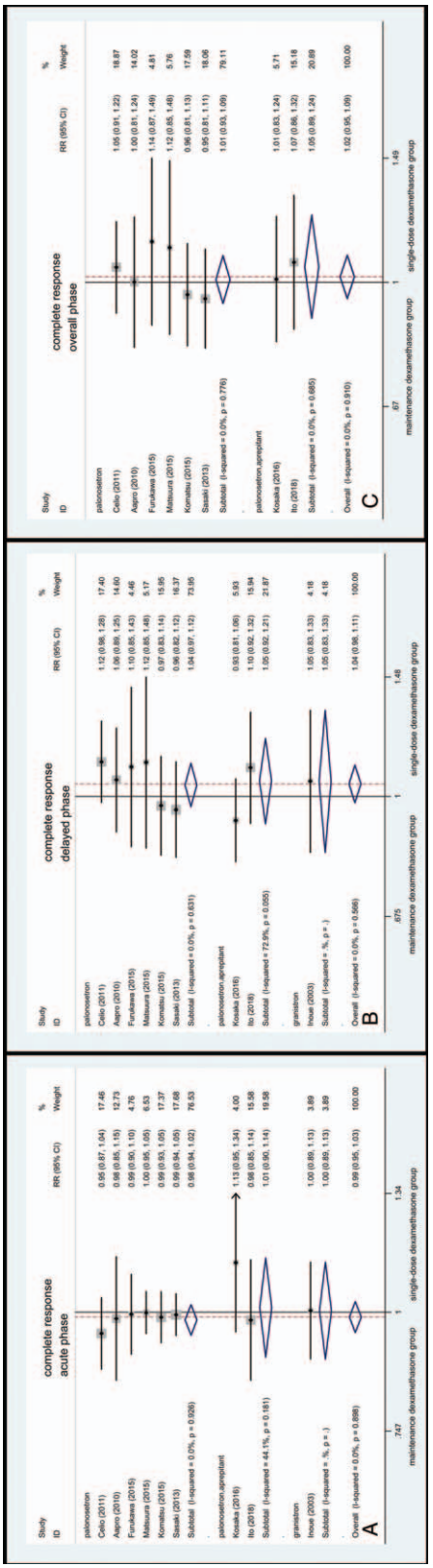

Figure 5. Forest plot for complete response of subgroup analysis of antiemetic regimens.

phases.[26] Studies which compared maintenance dexamethasone with single-dose dexamethasone were limited. This analysis was conducted to provide further evidence for the comparison.

Nausea and vomiting are both problems in CINV. We attached more importance to vomiting control as it is more objective to verify, values of nausea were relatively limited. The endpoints of this meta-analysis are no emesis, CR, CC, TC, and taking no rescue medications during the acute, delayed, or overall phase. Incidence of vomiting, CR, CC, and TC did not differ significantly between the maintenance dexamethasone and single-dose dexamethasone during the acute, delayed, or overall phase. Statistical significance favoring maintenance dexamethasone was attained in patients who did not use rescue medication.

The outcomes of present analysis suggest that patients in maintenance dexamethasone group have similar efficacy to those in single-dose dexamethasone group. However, maintenance dexamethasone regimen reduced the need for rescue analgesics when compared with single-dose dexamethasone regimen among the delayed ($P = .034$).

Some studies indicate that female or younger age is important risk factor for predicting a higher risk for CINV.[27,28] In this analysis, neither age nor sex was essentially associated with overall CR to anti-emetic treatment in subgroup analysis. However, the sample size was relatively limited.

Acute and chronic toxicity of dexamethasone comprise agitation, insomnia, increased appetite, weight gain, gastroesophageal reflux disease, and acne. Adverse effects are of interest but were inadequately reported. In most antiemetic studies, the adverse effects were recorded during the hospitalization. Also, it is difficult to determine whether the adverse effects were attributable to antiemetic treatment or maintenance dexamethasone. Furukawa et al[18] reported that patients accepting the maintenance dexamethasone prescription experienced a statistically significant but not severe higher incidence of insomnia. Vardy et al designed the questionnaire to evaluate the side effects associated with maintenance dexamethasone. In this study, patients experienced moderate to severe side effects with insomnia (45%), indigestion/epigastric discomfort (27%), agitation (27%), increased appetite (19%), weight gain (16%), and acne (15%), in the week following their chemotherapy.[29] The side effects of multiple-day dexamethasone may do more harm than good for patients receiving MEC.[29]

In our analysis, we performed the meta-analysis to evaluate the adverse effects. The incidence of hiccup was higher associated with maintenance dexamethasone. However, this value was recorded in an insufficient number of studies. Future trials should accurately concentrate on the side effects of dexamethasone so as to establish the overall safety of dexamethasone. Maintenance dexamethasone should not be applied in patients with a history of ulcers, hypertension, or diabetes.

Current guideline of NCCN (http://www.nccn.org) recommended that dexamethasone should be applied for several days to control CINV associated with HEC and MEC. In the guideline of MASCC/ESMO, a triple regimen consisting of maintenance dexamethasone plus a 5-HT3-receptor antagonist and an NK-1 receptor antagonist for the prevention of CINV owing to nonanthracycline/cyclophosphamide (AC)-based HEC agents was recommended.[30,31] In breast cancer patients treated with aprepitant, 5-HT3-receptor antagonist and dexamethasone on day 1, aprepitant or dexamethasone on day 2 and 3 were suggested.[31] In the guideline of ASCO, a 4-drug regimen consisting of 5-HT3-receptor antagonist, an NK-1 receptor antagonist, olanzapine, and dexamethasone was recommended to patients who are treated with HEC agents. Dexamethasone was only recommended on day 1 associated with AC-based HEC

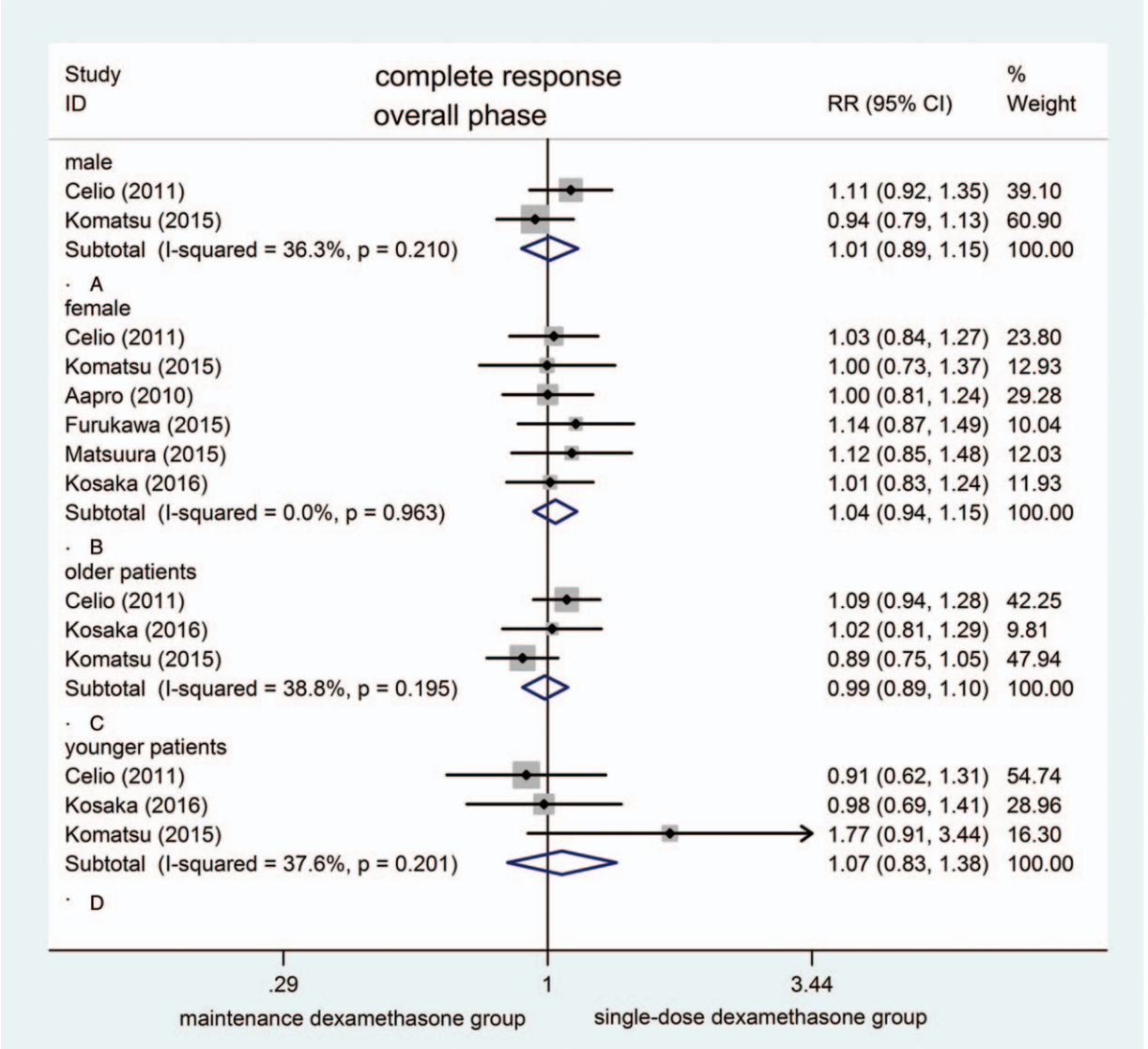

Figure 6. Forest plot for complete response of subgroup analysis of age categories and sex.

agents and was recommended on day 1 to 4 associated with other HEC agents.[32]

In the subgroup analysis of chemotherapy emetogenicities, we found that maintenance dexamethasone was not superior to single-dose dexamethasone in both HEC and MEC group during the acute, delayed, or overall phase. In the subgroup of antiemetic regimens analysis, antiemetic regimens consist of granisetron (one trial), palonosetron (6 trials), and palonosetron combined with aprepitant (2 trials). We found that maintenance dexamethasone was not superior to single-dose dexamethasone. Aprepitant was only applied in 2 studies which was recommended by guidelines.

In the guidelines of MASCC/ESMO and ASCO, patients who are treated with MEC agents that are known to cause delayed emesis may be recommended dexamethasone on days 2 to 3. This recommendation was based upon the study.[33] However, this study was conducted among the patients receiving AC (now considered HEC) single agent anthracycline, CMF, or carboplatin and it was unclear what percentage of enrolled patients received AC.[34]

Aprepitant has been demonstrated to be effective against CINV in both the acute and delayed phases.[35,36] However, there is no sufficient evidence to compare maintenance dexamethasone with single-dose dexamethasone when both are combined with NK-1 receptor antagonist directly. This analysis suggested that single-dose dexamethasone was effective. Additional studies are required to provide further evidence.

There is no doubt that dexamethasone is an effective and beneficial addition to anti-CINV regiments. In this analysis, we found single-dose dexamethasone regimen was an effective and safe alternative in antiemetic protection. These data may be of help to reduce the excessive utilization of dexamethasone, while still guaranteeing antiemetic effect and minimizing the side effect.

There are limitations among this study. One trials[21] included in this analysis was proceedings paper and only available for abstract. Only 9 clinical trials were reported to compare the efficacy of anti-CINV between maintenance dexamethasone and single-dose dexamethasone regimen. Aprepitant was only applied in 2 studies which was recommended for anti-CINV by all

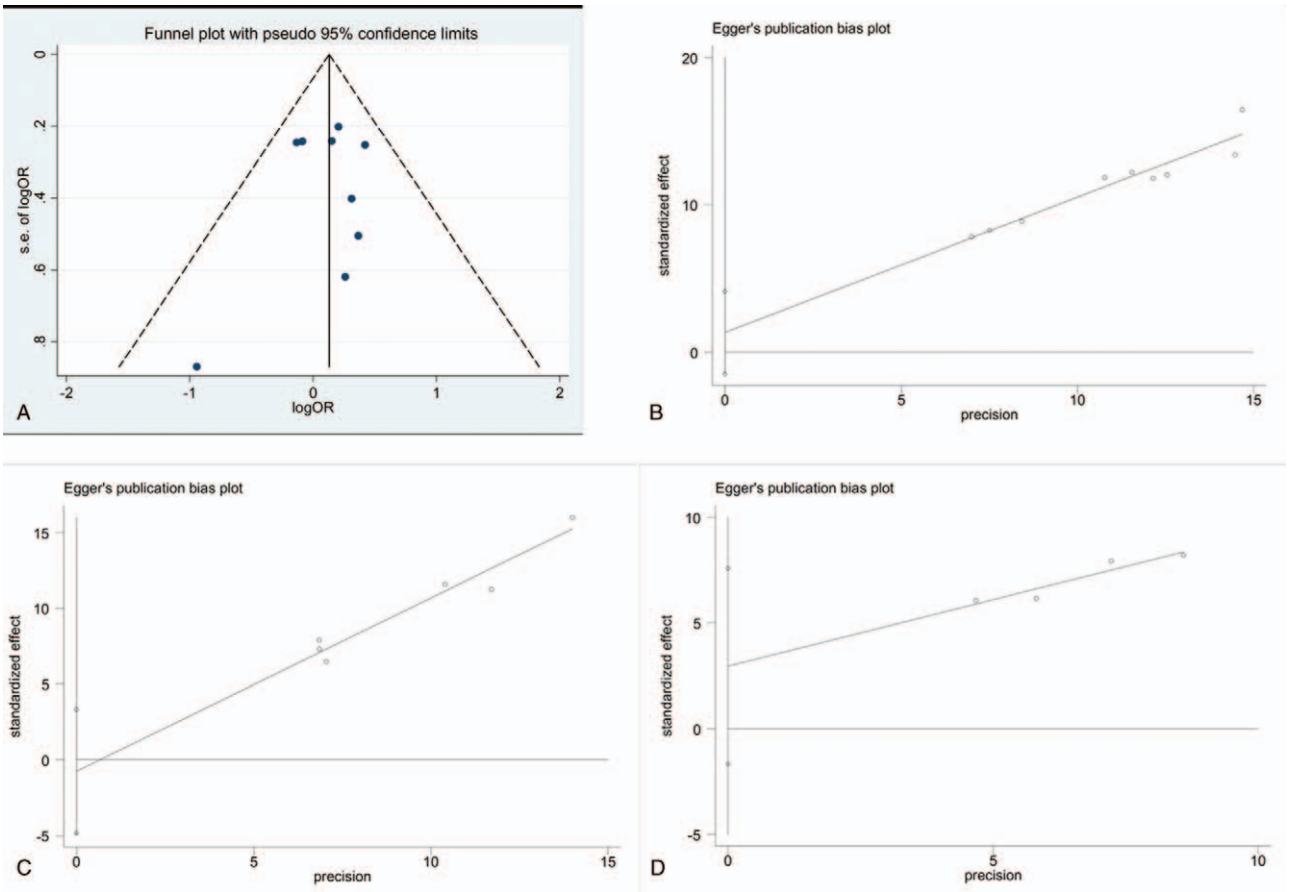

Figure 7. The funnel plot for complete response (A). Egger regression test for complete response (B). Egger regression test for complete control (C). Egger regression test for total control (D).

guidelines. CINV definition, types of chemotherapy and treatment options dramatically changed over the years, we excluded the studies before 2003.

The conclusion of this meta-analysis indicated that multiple-day dexamethasone was superfluous unless patients needed rescue medication. Our findings indicate that, irrespective of age, the single-dose dexamethasone regimen offers high and similar overall control of symptoms as the maintenance dexamethasone regimen in this population.

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Author contributions

Conceptualization: Jie Ren.
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