Systematic Review and Meta-Analysis

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Analgesic comparison of dezocine plus propofol versus fentanyl plus propofol for gastrointestinal endoscopy

A meta-analysis

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Abstract

Introduction: As the adjunctive anesthesia to propofol, both dezocine and fentanyl showed some potential for gastrointestinal endoscopy. This meta-analysis aimed to compare their efficacy and safety.

Methods: PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases were systematically searched. Randomized controlled trials (RCTs) assessing the effect of dezocine versus fentanyl for the anesthesia of patients undergoing gastrointestinal endoscopy were included.

Results: Five RCTs involving 677 patients were included in the meta-analysis. Overall, compared with fentanyl plus propofol for gastrointestinal endoscopy, dezocine plus propofol resulted in the reduction in propofol dose(mean difference [MD] = −11.72; 95% confidence interval [CI] = −22.83 to −0.61; $P = .04$), awakening time (std. MD = −1.79; 95% CI = −3.31 to −0.27; P = .02) and hypopnea (risk ratio [RR] = 0.16; 95% CI = 0.06–0.41; $P = .0002$), but had no remarkable effect on induction time (MD = 1.20; 95% CI = −0.98 to 3.39; $P = .28$), postoperative pain score (MD = −0.38; 95% CI = −1.00 to 0.24; $P = .24$), nausea or vomiting (RR = 0.45; 95% CI = 0.10–1.98; $P = .29$).

Conclusion: Dezocine plus propofol may be better for the anesthesia of gastrointestinal endoscopy than fentanyl plus propofol.

Abbreviations: CI = confidence interval, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RCTs = randomized controlled trials, SMD = standard mean difference.

Keywords: anesthesia, dezocine, fentanyl gastrointestinal endoscopy, meta-analysis

1. Introduction

Gastroscopy and colonoscopy are regarded as the common endoscopic methods for the diagnosis and treatment of gastrointestinal and colorectal diseases.[1–5] Gastroscopy aims to visualize the upper part of the gastrointestinal tract (ie, up to the duodenum), whereas colonoscopy is applied to observe the large intestine and the distal part of the small intestine.[3,6–8] Gastrointestinal endoscopy has become a well-established, highly effective diagnostic and therapeutic procedure for digestive diseases.[9,10] However, these endoscopy lead to some adverse reactions such as nervousness, nausea, vomiting, choking cough, and pain.[11,12] Severe discomfort may aggravate the preexisting condition or result in interruption of examination or treatment, such as the physiological dysfunction of some critically ill patients.[13,14]

The optimal methods for inducing analgesia and sedation in gastroscopy and colonoscopy remain the ongoing debate, and many experiment models are developed.[15] The administration of intravenous anesthetics is reported to effectively eliminate patient anxiety, inhibit upper airway reflex, and improve patient comfort during endoscopy.[16] Propofol as intravenous anesthetic in outpatient surgeries and examinations shows the features of enhanced depressant effects on the laryngeal reflexes, short action time, as well as rapid recovery profile,[17–19] but propofol as a single drug lacks the analgesic effects for a painless gastrointestinal endoscopy, and midazolam and remifentanil were applied to provide pain relief.[20,21]

Several studies have compared the analgesic efficacy of dezocine plus propofol with fentanyl plus propofol for gastrointestinal endoscopy, but there are some conflicting results.[22–24] Considering these inconsistent effects, we therefore

Editor: Sherif Ali.

The authors report no conflicts of interest.

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and material: Not applicable.

Funding: Not applicable.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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How to cite this article: Zhang L, Li C, Zhao C, Zhao Z, Feng Y. Analgesic comparison of dezocine plus propofol versus fentanyl plus propofol for gastrointestinal endoscopy: a meta-analysis. Medicine 2021;100:15(e25531).

Received: 19 March 2020 / Received in final form: 10 March 2021 / Accepted: 23 March 2021

http://dx.doi.org/10.1097/MD.0000000000025531

conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to investigate the efficacy and safety of dezocine plus propofol with fentanyl plus propofol for gastrointestinal endoscopy. Materials and methods, results, discussion, and conclusions were presented as follows.

2. Materials and methods

This systematic review and meta-analysis were conducted according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement[25] and the *Cochrane Handbook for Systematic Reviews of Interventions*.[26] All analyses are based on previous published studies; thus, no ethical approval and patient consent are required.

2.1. Literature search and selection criteria

PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases were systematically searched from inception to January 2019, with the following keywords: "Dezocine" AND "fentanyl" AND "propofol" AND "gastrointestinal endoscopy" (OR "gastroscopy" OR "colonoscopy"). To include additional eligible studies, the reference lists of retrieved studies and relevant reviews were also hand-searched and the process above was performed repeatedly until no further article was identified.

The inclusion criteria were as follows: study design was RCT, patients underwent gastrointestinal endoscopy, and intervention treatments were dezocine plus propofol versus fentanyl plus propofol.

2.2. Data extraction and outcome measures

The following information was extracted for the included RCTs: first author, publication year, sample size, baseline characteristics of patients, and detail methods of 2 groups. The author would be contacted to acquire the data when necessary. The primary outcomes were propofol dose and awakening time. Secondary outcomes included induction time, postoperative pain score, hypopnea, nausea, and vomiting.

2.3. Quality assessment in individual studies

The Jadad Scale was used to evaluate the methodological quality of each RCT included in this meta-analysis.[27] This scale consisted of three evaluation elements: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). One point would be allocated to each element if they have been mentioned in article, and another one point would be given if the methods of randomization and/or blinding had been appropriately described. The score of Jadad Scale varied from 0 to 5 points. An article with Jadad score ≤ 2 was considered to be of low quality. If the Jadad score ≥ 3, the study was thought to be of high quality.[28]

2.4. Statistical analysis

Standard mean differences (SMDs) or mean differences (MD0s) with 95% confidence intervals (CIs) for continuous outcomes (propofol dose, awakening time, induction time, and postoperative pain score) and risk ratio (RR) with 95% CIs for dichotomous outcomes (hypopnea, nausea, and vomiting) were used to estimate the pooled effects. Heterogeneity was quantified with the I^2 statistic, and the I^2 value $>50\%$ indicated significant heterogeneity. All meta-analyses were performed using random-effects models regardless of the heterogeneity. Sensitivity analysis was performed to detect the influence of a single study on the overall estimate via omitting one study in turn when necessary. Owing to the limited number (<10) of included studies, publication bias was not assessed. $P < .05$ in 2-tailed tests was considered statistically significant. All statistical analyses were performed with Review Manager Version 5.3 (The Cochrane Collaboration,Software Update, Oxford, UK).

3. Results

3.1. Study identification and selection

Figure 1 shows the diagram of meta-analysis search strategy and selection process. In all, 167 studies in the first search seemed to be potentially relevant. Finally, 5 articles were included in the meta-analysis.[22–24,29,30]

Table 1 showed the characteristics of the included studies. These studies were published between 2013 and 2019. The sample size varied from 60 to 200 patients with a total of 677. The 5 included studies involved gastroscopy,[29] colonoscopy,[23,30] and gastrointestinal endoscopy.[22,24] The combination of dezocine with propofol is compared with fentanyl and propofol in various doses.

Among the 5 RCTs, 4 studies reported propofol dose and awakening time,[22–24,30] 2 studies reported induction time,[22,24] and 3 studies reported postoperative pain score, hypopnea, nausea, and vomiting.[22–24] Jadad scores of the 5 included studies varied from 3 to 5, and all 5 studies were considered to be high-quality ones according to quality assessment.

3.2. Primary outcomes: propofol dose and awakening time

The pooled estimate of the included RCTs suggested that compared with fentanyl plus propofol for gastrointestinal endoscopy, dezocine plus propofol can significantly reduce propofol dose (MD = −11.72; 95% CI = −22.83 to −0.61; $P = .04$) with significant heterogeneity ($I^2 = 94\%$, heterogeneity $P < .00001$, Fig. 2) and awakening time (SMD = −1.79; 95% CI = −3.31 to −0.27; $P = .02$) with significant heterogeneity ($I^2 = 98\%$, heterogeneity $P < .00001$, Fig. 3). Intraoperative indexes were crucial to evaluate the analgesic efficacy of drugs including propofol dose, awakening time, induction time, and propofol dose among others.

3.3. Sensitivity analysis

Significant heterogeneity was observed for the primary outcomes. When performing sensitivity analysis by omitting one study in each turn to detect the source of heterogeneity, there was still significant heterogeneity. When we took subgroup analysis based on gastroscopy or colonoscopy, significant heterogeneity was still observed.

3.4. Secondary outcomes

In patients undergoing gastrointestinal endoscopy, dezocine plus propofol and fentanyl plus propofol demonstrated similar induction time (MD = 1.20; 95% CI = −0.98 to 3.39; $P = .28$; Fig. 4) and postoperative pain score (MD = −0.38; 95% CI = −1.00 to 0.24; $P = .24$; Fig. 5). Induction time was defined as the period it took for the patient to lose consciousness (from injection of propofol until the eyelash conditioned reflex disappeared).

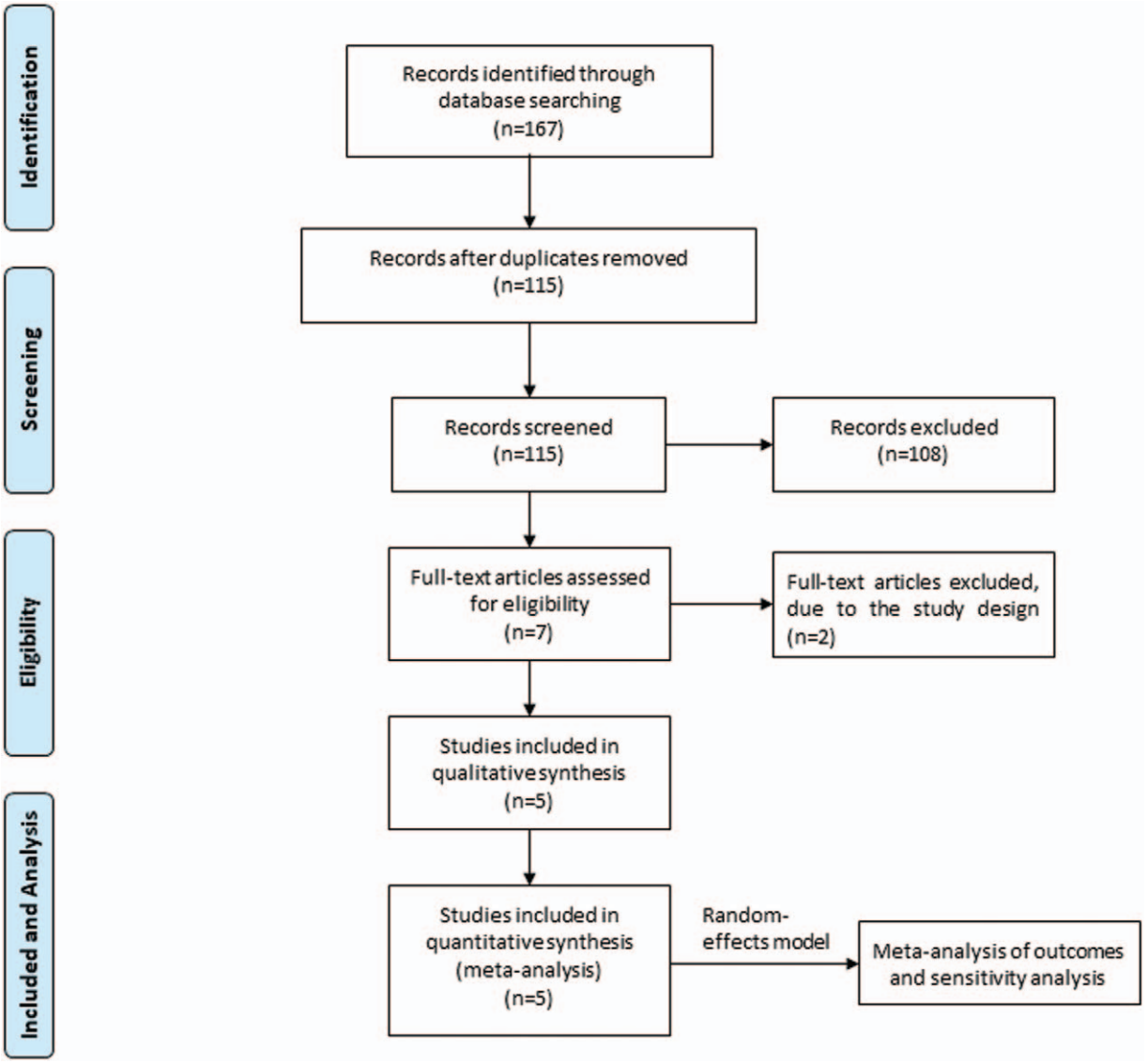

Figure 1. Flow diagram of study searching, selection process and analysis.

Pain intensity after the operation was assessed by postoperative pain score. These 2 outcomes were similar between 2 groups.

3.5. Adverse events

In comparison with fentanyl plus propofol for gastrointestinal endoscopy, dezocine plus propofol was associated with substantially reduced hypopnea (RR = 0.16; 95% CI = 0.06–0.41; $P = .0002$; Fig. 6), but showed no obvious effect on nausea or vomiting (RR = 0.45; 95% CI = 0.10–1.98; $P = .29$; Fig. 7). These indicated that fentanyl plus propofol may be better to reduce the respiratory depression than fentanyl plus propofol.

4. Discussion

It is well known that gastrointestinal endoscopy results in significant discomfort, nausea, vomiting, throat bleeding and anxiety. Anesthesia is required during the thorough examination,[31,32] but may produce some drawbacks such as delayed patient recovery and discharge time, hemodynamic instability, and increased risk of cardiopulmonary complications, particularly in elderly patients with cardiovascular diseases.[33,34] It is valuable and urgent to develop ideal anesthesia method for gastrointestinal endoscopy.

Propofol is widely used for the sedation of gastrointestinal endoscopy, but may cause marked depression on cardiovascular and respiratory parameters, loss of protective reflexes, especially in elderly patients.[17–19] Especially, there is lack of analgesic effect of propofol, and thus the use of propofol in combination with opioids is found to improve sedation and analgesia with regard to recovery time, sedative effect, pain, and discomfort.[35,36]

In addition, etomidate plus propofol is more effective for the analgesia of gastroscopy, and with fewer influence on respiration and circulation for patients undergoing gastroscopy than propofol alone.[37] Considering the analgesic comparison of dezocine with fentanyl as the adjunctive treatment to propofol for gastrointestinal endoscopy, there are some conflicting results.[22–24]

Table 1

Characteristics of included studies.

No.	Author	Operation type	Dezocine group						Fentanyl group						Jada scores
			No.	Age, y	Female (n)	Body weight, kg	Operation time, min	Methods	No.	Age, y	Female (n)	Body weight, kg	Operation time, min	Methods	
1	Li et al, 2019[22]	Gastroscopy, colonoscopy	100	51 ± 20	52	76 ± 15	46 ± 9	Intravenous 1.0–2.5 mg/kg propofol + 0.05 mg/kg dezocine	100	53 ± 19	49	72 ± 16	45 ± 9	1.0–2.5 mg/kg propofol + 1.0 μg/kg fentanyl	5
2	Li et al, 2017[29]	Gastroscopy	67	42–65	25	—	—	Intravenous injection of 5 mg dezocine, 1–2 mg/kg propofol, as well as intraoperative micro-pump injection of 2–4 mg/kg/h propofol	67	44-63	27	—	—	Intravenous injection of 0.05 mg fentanyl, 1–2 mg/kg propofol and intraoperative micro-pump injection of 2–4 mg/kg/h propofol	3
3	Yang et al, 2014[23]	Colonoscopy	83	40.82 ± 5.13	29	60.06 ± 4.77	23.08 ± 8.31	Dezocine 5 mg + propofol 1.5–2.0 mg/kg	100	41.57 ± 5.76	28	61.12 ± 3.92	25.71 ± 7.83	Fentanyl 0.5 μg/kg + propofol 1.5–2.0 mg/kg	4
4	Wang 2014	Gastrointestinal endoscopy	50	63.74 ± 5.24	—	61.85 ± 10.09	—	Dezocine 0.1mg + propofol 2–3 mg/kg	50	63.82 ± 5.05	—	62.05 ± 10.55	—	Fentanyl 1 μg/kg + propofol 2–3 mg/kg	4
5	Zhang et al, 2013[23]	Colonoscopy	30	31–65	—	51–75	—	Dezocine 5mg + propofol 1.0–2.0 mg/kg	30	31–65	—	51–75	—	Fentanyl 0.05 mg + propofol 1.0–2.0 mg/kg	4

The combination of propofol and dezocine supplementation at the dose of 0.05 mg/kg could decrease propofol dosage, shorten awakening time, reduce postoperative pain score, decrease inhibitory effects on the respiratory and cardiovascular systems than fentanyl supplementation for gastroscopy and colonoscopy.[22] The rates of apnea, postoperative nausea, vomiting and dizziness were also found to be lower in dezocine supplementation group than those in fentanyl supplementation group.[23] However, another RCT revealed similar mean atrial pressure, heart rate, respiratory rate and SpO2 between two groups for gastrointestinal endoscopy.[24] Our meta-analysis suggested that dezocine plus propofol is associated with the significant reduction in propofol dose, awakening time and hypopnea compared to fentanyl plus propofol for gastrointestinal endoscopy, but comparable induction time, postoperative pain score, nausea, and vomiting are observed between 2 groups.

Significant heterogeneity was observed for the primary outcomes. When performing sensitivity analysis by omitting one study in each turn to detect the source of heterogeneity, there was still significant heterogeneity. When we took subgroup analysis based on gastroscopy or colonoscopy, significant heterogeneity was still observed. There are three reasons for explaining the significant heterogeneity. First, the 5 included studies involved gastroscopy,[29] colonoscopy,[23,30] and gastrointestinal endoscopy.[22,24] Different procedures and pain intensity are included in gastroscopy and colonoscopy. Secondly, various dosages and methods of drug administration are applied, which may form different levels of analgesic efficacy. Thirdly, the combination drug propofol is used at various doses, which may affect the pooling results.

Several limitations should be taken into account. First, our analysis was based on only 5 RCTs involving 677 patients and more studies with large patient sample are needed to explore this issue. Secondly, there was significant heterogeneity, which may be caused by different operation type (ie, gastroscopy, colonoscopy, and gastrointestinal endoscopy), dosages (eg, 0.5–1.0 μg/kg fentanyl), and methods of drug administration. Finally, the combination drug propofol was used at various doses (1.0–3.0 mg/kg), and the pooling results may be affected.

5. Conclusions

Our meta-analysis included only 5 RCTs involving 677 patients. The results revealed that dezocine plus propofol is associated with the significant reduction in propofol dose, awakening time and hypopnea compared to fentanyl plus propofol for gastrointestinal endoscopy, but comparable induction time, postoperative pain score, nausea, and vomiting were observed between 2 groups. Significant heterogeneity remained, and may be caused by three reasons. First, different procedures and pain intensity (ie, gastroscopy, colonoscopy, and gastrointestinal endoscopy) was included among the included RCTs. Secondly, various dosages and methods of drug administration were applied, which may form different levels of analgesic efficacy. Thirdly, the combination drug propofol is used at various doses, which may affect the pooling results. In addition, our analysis was based on only 5 RCTs involving 677 patients and more studies with large patient sample are needed to explore this issue. As the adjunctive analgesia to propofol for gastrointestinal endoscopy, dezocine at the dose of 5 mg may be preferred over fentanyl.

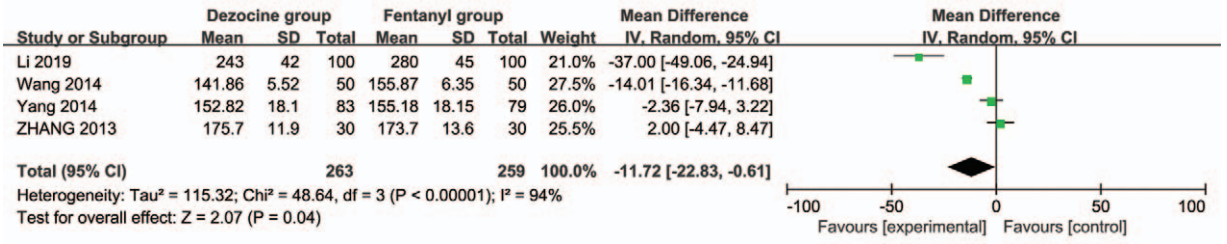

Figure 2. Forest plot for the meta-analysis of propofol dose (mg).

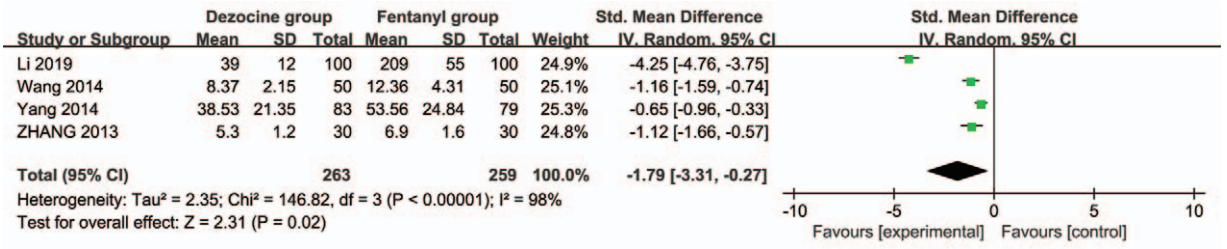

Figure 3. Forest plot for the meta-analysis of awakening time (s).

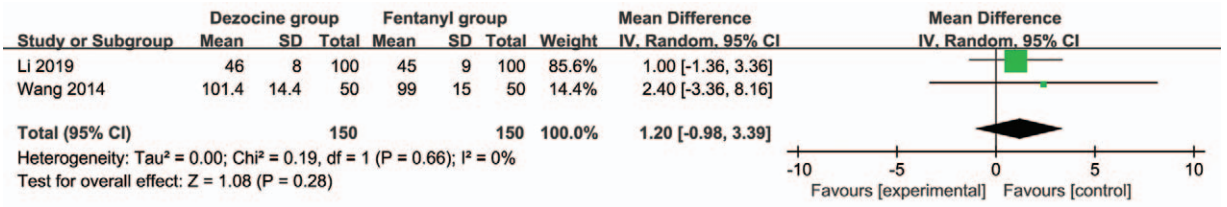

Figure 4. Forest plot for the meta-analysis of induction time (s).

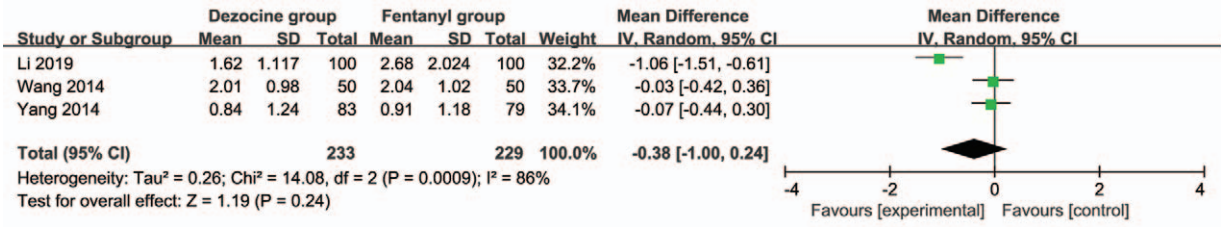

Figure 5. Forest plot for the meta-analysis of postoperative pain score.

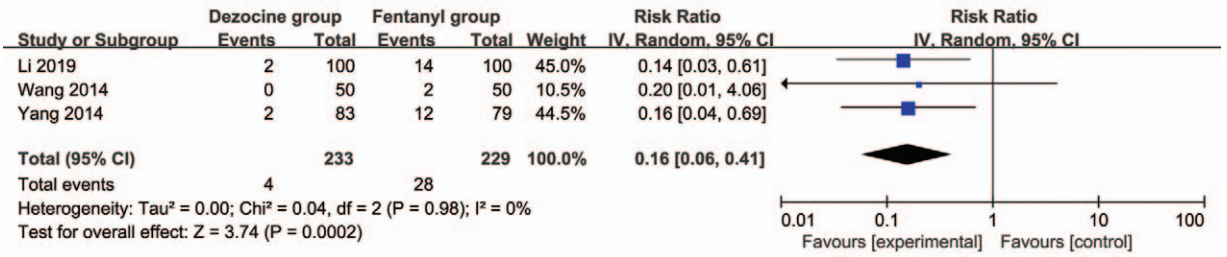

Figure 6. Forest plot for the meta-analysis of hypopnea.

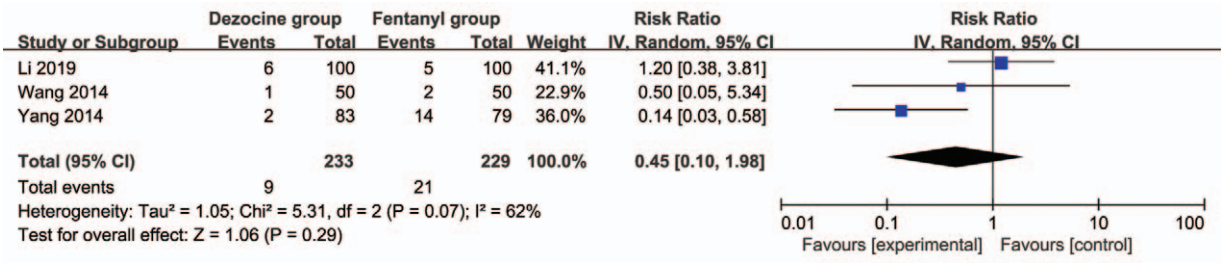

Figure 7. Forest plot for the meta-analysis of nausea and vomiting.

Author contributions

All authors make equally to this work.
Conceptualization: Lin Zhang, Yi Feng.
Data curation: Yi Feng.
Formal analysis: Lin Zhang.
Funding acquisition: Chun Li.
Project administration: Chuncheng Zhao.
Software: Chuncheng Zhao.
Supervision: Zhengzhong Zhao.
Writing – original draft: Yi Feng.

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