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Original Article

Efficacy of dexmedetomidine on postoperative nausea and vomiting: a meta-analysis of randomized controlled trials

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Abstract: Purpose: Postoperative nausea and vomiting (PONV) is a frequent complication in postoperative period. The aim of the current meta-analysis was to assess the efficacy of dexmedetomidine on PONV. Methods: Two researchers independently searched PubMed, Embase and Cochrane Central Register of Controlled Trials for randomized controlled trials (RCTs). The meta-analysis was performed with Review Manager. Results: Eighty-two trials with 6,480 patients were included in this meta-analysis. Dexmedetomidine reduced postoperative nausea (Risk Ratio (RR) = 0.61, 95% confidence interval (CI): 0.50 to 0.73) and vomiting (RR = 0.48, 95% CI: 0.36 to 0.64) compared with placebo, with an effective dose of 0.5 μg/kg (RR = 0.46, 95% CI: 0.34 to 0.62) and 1.0 μg/kg (RR = 0.29, 95% CI: 0.12 to 0.75), respectively. The antiemetic effect can only be achieved intravenously, not epidurally or intrathecally. The efficacy of dexmedetomidine was similar to that of widely used agents, such as propofol, midazolam etc., but better than opioid analgesics. Moreover, application of dexmedetomidine reduced intraoperative requirement of fentanyl (Standard Mean Difference = -1.91, 95% CI: -3.20 to -0.62). Conclusions: The present meta-analysis indicates that dexmedetomidine shows superiority to placebo, but not to all other anesthetic agents on PONV. And this efficacy may be related to a reduced consumption of intraoperative opioids.

Keywords: Dexmedetomidine, meta-analysis, nausea, vomiting

Introduction

Postoperative nausea and vomiting (PONV) are unwished outcomes after sedation or anesthesia, which can result in unplanned admission or delay hospital discharge [1]. Meanwhile vomiting can stress wounds, cause electrolyte imbalance and bleeding [2]. Therefore patients rate PONV as one of the least desirable events after surgeries [3], especially laparoscopy, laparotomy, and strabismus surgeries [4]. Additionally, four clear risk factors have been shown to independently predict PONV: female gender, postoperative opioid treatment, prior history of motion sickness and/or PONV and non-smoker, which increased risk by 20% respectively [5]. The risks of PONV may also vary with: preanaesthetic medication, anesthetic techniques, postoperative pain management [1].

Dexmedetomidine, with sedative, analgesic [6], sympatholytic and amnestic [7] properties is a potent and highly selective α_2-adrenoceptor agonist, which binds to transmembrane G protein-binding receptor, and has no activity on the γ-aminobutyric acid (GABA) system [8]. And clinical researchers have already studied the administration of dexmedetomidine to prevent PONV. Nevertheless, controversy about the effectiveness of dexmedetomidine for the arrest of PONV is still ongoing, for different results reported in associated literature.

To our knowledge, there was no quantitative analysis done for the combination of related data primarily. Therefore, we conducted the current meta-analysis aiming to explore the use of dexmedetomidine as an efficacious antiemetic agent.

Methods

This meta-analysis aiming to assess the role of dexmedetomidine on PONV was performed decently according to the recommendations of the PRISMA statement. Because nausea and vomiting were defined as two separate phenomena, studies should report and evaluate the variables distinctly [9]. While since few patients experience vomiting without nausea, the incidence of PONV and postoperative nausea (PON) is fairly similar, thus original papers often do not try to distinguish these variables [10]. So, if PONV but not PON was reported in trails, we considered the PONV variables as a very close substitute for PON; when both PONV and PON were reported simultaneously, we assessed the nausea values. The most commonly used time interval to measure the role of antiemetic is 24 hours [9]. When only longer or shorter time interval was reported, we used the time interval which was closest to the 24-hour interval.

Search strategy

Two authors (L.X. and Z.M.) systematically searched Cochrane Central Register of Controlled Trials (CENTRAL), Embase and PubMed. The search strategy comprised the following key words: (dexmedetomidine) and (nausea, vomiting or PONV) and (anaesthesia, anesthesia, surgery, operation or postoperative). The literature search was updated on December 31, 2014 with no language limitation. The reference lists of the reviews, original reports and case reports (retrieved through the electronic searches) were checked to identify studies that had not yet been included in the computerized databases.

Study selection and data retrieval

The study selection criteria were pre-established. Inclusion criteria: (1) Randomized controlled trial; (2) The administration of dexmedetomidine preoperatively, intraoperatively or postoperatively; (3) The presence of nausea or vomiting reported; (4) Dexmedetomidine versus placebo or a single agent. Exclusion criteria: (1) Duplications or abstracts only; (2) Missing data; (3) Patients with severe cerebrovascular disease or other contraindications of dexmedetomidine; (4) Incorrect statistical analysis performed in the report; (5) Agent/agents (including dexmedetomidine) versus combinational agents. Data retrieval: name of the first author, publication year, funding, interventions, patients, type of anesthesia and surgery, length of operation, number of nausea and vomiting cases and total patients. Two authors (L.X. and Z.M.) independently assessed the articles for compliance with the inclusion/exclusion criteria. Any of disputes about this meta-analysis was settled promptly by discussion among all of the authors.

Qualitative assessment

Two authors (F.J.J. and W.L.) evaluated the quality of the trials independently according to the guideline recommended by the Cochrane Collaboration [11]. Six categories (randomization sequence generation, blinding method, allocation concealment, incomplete outcome data, selective reporting, other bias, with the first three categories considered as "key domains") were assessed, each one summarized into three levels: high risk, unclear risk, and low risk. The risk of bias of each study was evaluated according to the levels of the three key domains: "High" (high risk of bias for one or more key domains), "Unclear" (unclear risk of bias for one or more key domains), and "Low" (low risk of bias for all key domains).

Statistical analysis

The efficacy of dexmedetomidine on nausea and vomiting, compared with placebo or other anesthetic drugs, was estimated by calculating pooled Risk Ratio (RR), and the consumption of intraoperative fentanyl was assessed by pooled Standard Mean Difference (SMD), with 95% confidence intervals (CI). The overall effect was determined by Z test ($P < 0.05$ was considered statistically significant). A fixed effects model was adopted when $I^2 \leq 50\%$, otherwise, a random effects model was used.

Sensitivity analysis was performed to test the robustness of these results, by reanalyzing the data of low-risk and unclear-risk studies only. Subgroup analyses were based on the type of anesthesia, route of administration, investigator initiated trail, dosage regimen, dose of dexmedetomidine, high-risk factor of PONV and other anesthetic agents.

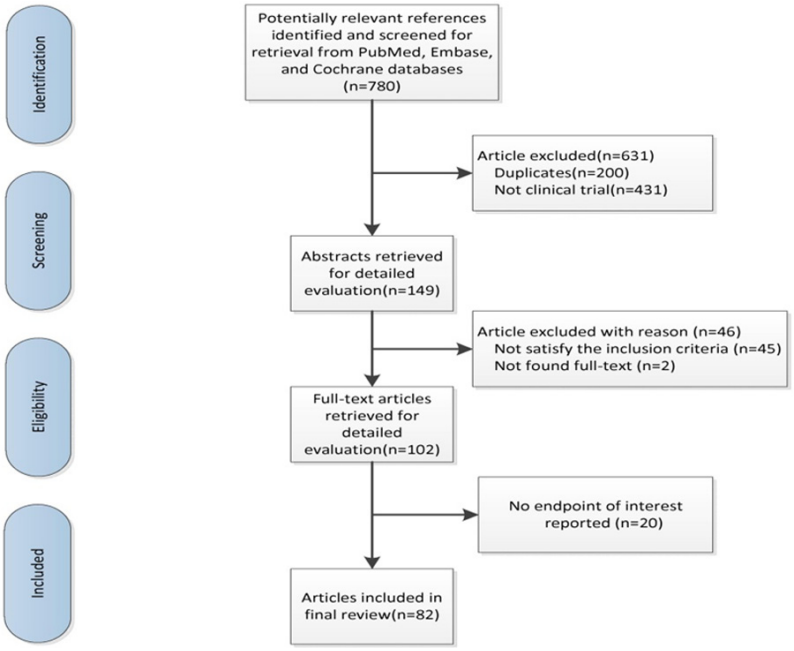


Figure 1. Flow diagram of the inclusion and exclusion process.

Begg's Test was conducted to assess potential publication bias. Statistical analysis was performed with Stata® (Version 12.0; Stata Corp, TX, USA) and Review Manager (RevMan®) (Version 5.3; The Cochrane Collaboration, Oxford, UK).

Result

Study selection

As shown in the flow diagram (**Figure 1**), the search of PubMed, Embase, CENTRAL and reference lists yielded 780 articles. Initially, 431 trials were discarded because they were not controlled trials by reading the titles. Then, 46 were excluded for not relevant to our study by reviewing the abstracts. Two full-texts [12, 13] of the remaining 104 papers couldn't be retrieved in spite of efforts by interlibrary loan, electric retrieval and contacting the authors. One hundred and two papers were carefully read, and we found no related endpoints were reported in 20 papers, so they were excluded. Finally, 82 trials [14-95] that met the selection criteria were included in the meta-analysis.

Study characteristic

Of all the included studies, 49 trials [14-62] explored the efficacy of dexmedetomidine compared with placebo. Other control agents included fentanyl [23, 48, 68, 73, 78, 80, 86, 87, 93], remifentanyl [77, 82, 84, 91, 95], morphine [69, 72, 81, 83], propofol [34, 63, 67, 70, 88, 94], midazolam [65, 66, 74, 76, 85, 89, 90], clonidine [44, 79, 92], ketamine [18, 32, 35], buprenorphine [71], lefoxidine [75], $MgSO_4$ [16], thiopental [46]. Only 32 of the included articles clearly mentioned the funding status, 12 of which [14, 22, 25, 27, 38, 39, 41, 43, 51, 73, 74, 77] were supported by institutional foundation, and 20 studies [17, 19-21, 30, 32-35, 40, 42, 49, 56, 61, 64, 66-68, 78, 79] declared no financial supports (**Table 1**).

The methodological quality of the included studies

Sixty-nine [14, 16-21, 23-37, 39-43, 45-53, 56, 58-62, 64-67, 69, 71-90, 92-95] of the 82 included trials provided a detailed description of randomization. Odd/even admission number was used in the process of randomization in one trial [54]. Fifty-seven studies [17, 18, 21, 23-26, 28-34, 37, 39-49, 51, 52, 54, 55, 57-59, 61, 62, 64, 65, 67, 69, 72, 73, 76, 77, 79, 81-90, 92, 95, 96] were double-blinded; 59 trials [16-21, 23-26, 29, 30, 32, 33, 35-37, 39-42, 44-47, 49, 52-60, 62, 64-69, 73, 76, 77, 79, 81-89, 92, 93, 95, 96] reported allocation concealment. All the studies had no incomplete outcome (attrition bias) and all the studies reported all the end points mentioned in the Methods section (reporting bias). Other bias might exist in six trials [40, 43, 66, 74, 83, 94] (the type of surgery was not clear). An overview of the risk of bias is summarized in **Figure 2**.

Results of meta-analysis

Dexmedetomidine vs. placebo: Forty-three trials [14-31, 35-42, 44-47, 49-61], including 2,486 patients, investigated the efficacy of preventing nausea, meanwhile vomiting was detected in 27 trails [17, 21-25, 29, 31-35, 38, 40, 43, 45, 47-52, 55, 56, 60-62] including 1,575 patients, by comparing dexmedeto-

Table 1. Characteristics of the included trials

author	Year	Participants	Type of anesthesia	Type of surgery	Trail	Dosage regimen	Comparisons	Total	nausea	vomiting	Operation time (Mean ± SD or median, min.)	Funding
Zhao [14]	2014	adults	GA	Thyroidectomy	I	S	dexmedetomidine IV 0.4 μg/kg	30	0	-	150.4±15.6	①
							dexmedetomidine IV 0.8 μg/kg	30	0	-	152.7±15.2	
							placebo IV	30	4	-	148.5±14.6	
Yektas [15]	2014	adults	SA	inguinal surgery	I	S	dexmedetomidine SA 2 μg	20	4	-	-	-
							dexmedetomidine SA 4 μg	20	5	-		
							placebo SA	20	2	-		
Shahi [16]	2014	adults	EA	lower limb surgery	I	S	dexmedetomidine EA 0.5 μg/kg	40	6	-	-	-
							$MgSO_4$ EA 50 mg	40	3	-		
							placebo	40	4	-		
Nie [17]	2014	adults	SA	elective caesarean delivery	E	S	dexmedetonidine IV 0.5 μg/kg	40	1	0	40.2±7.5	No
							placebo IV	38	2	0	39.2±6.7	
Gyanesh [18]	2014	children	GA	MRI examination	I	C	dexmedetomidine IV	52	2	-	18±5	-
							ketamine IV	52	5	-	18±6	
							placebo IV	46	3	-	19±6	
Dinesh [19]	2014	adults	SA	inguinal hernia repair, vaginal hysterectomy, arthroscopic ACL tear repair	I	L	dexmedetomidine IV	50	2	-	140.9±33.4	No
							placebo IV	50	0	-	137.2±33.1	
Almarakbi [20]	2014	adults	PNB	abdominal hysterectomy	I	L	dexmedetomidine PNB	25	1	-	72.6±7.5	No
							Placebo PNB	25	2	-	74.5±9.1	
Agarwal [21]	2014	adults	PNB	upper limb surgeries	I	L	dexmedetomidine PNB	25	0	0	-	No
							placebo PNB	25	0	0		
Wu [22]	2013	adults	GA	laparoscopic surgery	E	S	dexmedetomidine IV 1.0 μg/kg	40	1	1	94.62±5.28	②
							placebo IV	40	5	4	92.16±6.36	
Tarbeeh [23]	2013	adults	SA	lower limb orthopedic surgery	I	L	dexmedetomidine SA 10 μg	20	1	0	-	-
							fentanyl SA 25 μg	20	1	2		
							placebo SA	20	0	0		
Shin [24]	2013	adults	GA	laparoscopically assisted vaginal hysterectomy, total abdominal hysterectomy, ovarian surgery	I	S	dexmedetomidine IV 1.0 μg/kg	21	2	0	-	-
							placebo IV	21	3	0		
Mizrak [25]	2013	children	GA	adenotonsillectomy	I	S	dexmedetomidine IV 0.5 μg/kg	30	2	0	22.7±4.05	③
							placebo IV	30	3	0	24.3±5.5	
Mazanikov [26]	2013	adults	GA	endoscopic retrograde cholangiopancreatography	I	L	dexmedetomidine IV	25	2	-	22±12	-
							placebo IV	25	1	-	25±14	
Lee [27]	2013	adults	GA	laparoscopically assisted vaginal hysterectomy	I	L	dexmedetomidine IV	28	1	-	-	④
							placebo IV	29	8	-		
Kim a [29]	2013	adults	GA	uterine artery embolization	I	C	dexmedetomidine IV 0.2 μg/kg/h	25	8	8	43±8	-

							placebo IV	25	5	18	42±8	
Kim b [28]	2013	adults	GA	modified radical mastectomy	I	S	dexmedetomidine IV 0.5 ug/kg	46	18	-	120	-
							placebo IV	46	26	-	118	
Gupta [30]	2013	chiildren	GA	corrective surgery	I	L	dexmedetomidine IV	18	2	-	165.3±77.7	No
							placebo IV	18	9	-	122±36.7	
Esmaoglu [31]	2013	adults	SA	transurethral endoscopic surgery	I	L	dexmedetomidine SA	30	2	1	58.5±21.9	-
							placebo SA	30	1	1	56.3±22.5	
Chen [32]	2013	children	GA	elective strabismus surgery	I	L	dexmedetomidine IV	27	-	4	35.8±7.3	No
							ketamine IV	27	-	12	34.6±7.5	
							placebo IV	24	-	11		
Bindu [33]	2013	adults	GA	elective general surgical, urological and gynecological surgeries	E	S	dexmedetomidine IV 0.75 ug/kg	25	-	1	-	No
							placebo IV	25	-	2		
Ali [34]	2013	children	GA	adenotonsillectomy	E	S	dexmedetomidine IV 0.3 ug/kg	40	-	4	36.7±10.8	No
							propofol IV 1 mg/kg	40	-	5	38.6±12.2	
							placebo IV	40	-	3	35.0±9.8	
Singh [35]	2012	adults	GA	laparoscopic surgical procedures	E	S	dexmedetomidine IV 1 ug/kg	40	2	1	59.14±4.28	No
							placebo	40	7	4	57.86±5.68	
Jain [36]	2012	adults	SA	elective lower limb orthopaedic surgery	I	S	dexmedetomidine EA 2 ug/kg	30	0	-	80.9	-
							placebo EA	30	0	-	79.3	
Hong [37]	2012	adults	SA	transurethral resection of the prostate	I	S	dexmedetomidine IV 1.0 ug/kg	26	2	-	31.2±18.4	-
							placebo IV	25	1	-	28.2±13.3	
Wu [38]	2011	adults	GA	total hip replacement	Po	C	dexmedetomidine IV 0.2 ug/(kg·h)	20	1	0	121±28	⑤
							placebo IV	20	6	5	116±23	
Ohtani [39]	2011	adults	GA	open gynecological abdominal surgery	I	C	dexmedetomidine IV	16	3	-	250±66	⑥
							placebo IV	16	2	-	233±69	
Gupta a [40]	2011	adults	SA	lower limb surgeries	I	S	dexmedetomidine SA 5 ug	30	1	0	-	No
							placebo SA	30	2	0		
Cheung [41]	2011	adults	GA	bilateral third molar surgery	I	S	dexmedetomidine IV 1 ug/kg	33	8	-	50.5±18.6	⑦
							placebo IV	33	4	-	56.7±23.8	
Abdelmageed [42]	2011	adults	GA	uvulopalatopharyngoplasty	E	L	dexmedetomidine IV	20	7	-	74±43	No
							placebo IV	19	14	-	78±49	
Sato [43]	2010	children	GA	pediatric ambulatory surgery	I	S	dexmedetomidine IV 0.3 ug/kg	39	-	3	49±38	⑧
							placebo IV	42	-	3	41±32	
Neogi [44]	2010	children	EA	elective inguinal herniotomy	I	S	dexmedetomidine EA 1 ug/kg	25	3	-	39±9.43	-
							clonidine EA 1 ug/kg	25	2	-	38±7.8	
Mizrak a [46]	2010	adults	GA	inguinal hernia, laparoscopic cholecystectomy, breast biopsy	I	S	dexmedetomidine IV 0.5 ug/kg	30	5	-	60±13.4	-

							thiopental IV 1 mg/kg	30	4	-	62.5±12.2	
							placebo IV	30	8	-	64.5±14.2	
Mizrak b [45]	2010	adults	IVRA	carpal tunnel release	I	S	dexmedetomidine IV 0.5 ug/kg	15	0	0	45±19	-
							placebo IV	15	0	0	38±17	
Elcicek [47]	2010	adults	SA	lower extremity surgery	I	L	dexmedetomidine IV	30	3	0	-	-
							placebo IV	30	2	0		
Massad [49]	2009	adults	GA	elective diagnostic laparoscopic surgeries	I	C	dexmedetomidine IV 0.5 ug/kg/h	42	8	5	30.5±3.1	No
							placebo IV	39	15	8	28.4±2.2	
Erdil [48]	2009	children	GA	adenoidectomy	I	S	dexmedetomidine IV 0.5 ug/kg	30	-	1	38.7±17.1	-
							fentanyl IV 2.5 ug/kg	30	-	3	36.2±16.8	
							placebo IV	30	-	1	35.8±18.3	
Turan [50]	2008	adults	GA	elective intracranial surgery	E	S	dexmedetomidine IV 0.5 ug/kg	20	0	0	256±49	-
							placebo IV	20	0	0	251±46	
Tufanogullari [51]	2008	adults	GA	laparoscopic bariatric surgery	I	C	dexmedetomidine IV 0.8 ug/kg/h	20	9	2	111±56	⑨
							dexmedetomidine IV 0.4 ug/kg/h	20	6	0	107±35	
							dexmedetomidine IV 0.2 ug/kg/h	20	5	1	110±62	
							placebo IV	20	13	3	116±52	
Goksu [52]	2008	adults	LA	functional endoscopic sinus surgery	I	L	dexmedetomidine IV	30	5	3	-	-
							placebo IV	32	25	13		
Elvan [53]	2008	adults	GA	elective total abdominal hysterectomy	I	L	dexmedetomidine IV	40	2	-	78.3±19.7	-
							placebo IV	40	2	-	81.9±28.2	
Tekin [54]	2007	-	SA	lower abdominal, anorectal, or extremity surgery	I	L	dexmedetomidine IV	30	0	-	71.02±13.58	
							placebo IV	30	0	-	72.50±14.84	
Bakhamees [55]	2007	adults	GA	elective laparoscopic Roux-en-Y gastric bypass surgery	I	L	dexmedetomidine IV	40	2	0	157±29	-
							placebo IV	40	3	0	155±27	
Yildiz [56]	2006	adults	GA	elective minor surgery	I	S	dexmedetomidine IV 1 ug/kg	25	6	3	-	No
							placebo IV	25	10	9		
Ozkose [57]	2006	adults	GA	elective surgery for lumbar disc disease	I	L	dexmedetomidine IV	20	2	-	98.35±27.4	-
							placebo IV	20	3	-	90.8±20.2	
Isik [58]	2006	children	GA	magnetic resonance imaging examination	I	S	dexmedetomidine IV 1 ug/kg	21	1	-	44.4±20.9	-
							placebo IV	21	2	-	39.3±8.4	
Gurbet [59]	2006	adults	GA	total abdominal hysterectomy	I	L	dexmedetomidine IV	25	6	-	101±25	-
							placebo IV	25	15	-	109±25	
Cicek [60]	2006	adults	GA	septorhinoplasty	I	L	dexmedetomidine IV	25	8	4	183±37	-
							placebo IV	25	11	6	186±47	
Unlugenc [61]	2005	adults	GA	elective abdominal surgery	I	S	dexmedetomidine IV 1 ug/kg	30	2	0	-	No

							plcebo IV	30	4	0		
Guler [62]	2005	children	GA	adenotonsillectomy	E	S	dexmedetomidine IV 0.5 ug/kg	30	-	11	35.73±8.3	-
							plcebo IV	30	-	16	37.63±5.6	
Verma [63]	2014	adults	LA	tympanoplasty	I	L	dexmedetomidine IV	39	4	2	44.9±5.3	-
							propofol IV	37	3	1	46.8±6.07	
Singh [64]	2014	children	GA	dental procedures	I	S	dexmedetomidine IV 3 ug/kg	28	-	0	-	No
							dexmedetomidine IV 4 ug/kg	28	-	0	-	
Sheta [65]	2014	children	GA	complete dental rehabilitation	I	S	dexmedetomidine IN 1 ug/kg	36	6	-	112.1±18.8	
							midazolam IN 0.2 mg/kg	36	5	-	107.5±20.8	
Sethi [66]	2014	adults	GA	endoscopic retrograde cholangiopancrea-tography	I	L	dexmedetomidine IV	30	-	2	-	No
							midazolam IV	30	-	4		
Peng [67]	2014	children	GA	cerebral angiography	I	L	dexmedetomidine IV	31	0	-	31.2±11.2	No
							propofol IV	31	1	-	35.8±10.7	
Manuar [68]	2014	adults	SA	arthroscopic knee surgery	E	S	dexmedetomidine IA 100 ug	33	0	0	115.30±16.343	No
							fentanyl IA50 ug	33	0	0	111.36±14.046	
							ropivacaine IA 75 mg	33	0	0	112.27±15.211	
Kamal [69]	2014	adults	EA	major abdominal surgery	I	S	dexmedetomidine EA 1.5 ug/kg	30	5	3	-	-
							morphine EA 1 mg	30	10	8		
Hasanin [70]	2014	children	GA	gastrointestinal endoscopy	I	L	dexmedetomidine IV	40	-	0	20.70±10.71	-
							propofol IV	40	-	1	19.65±7.69	
Gupta [71]	2014	adults	SA	elective lower abdominal surgeries	I	S	dexmedetomidine SA 5 ug	30	4	-	-	-
							buprenorphine SA 60 ug	30	2	-		
El Shamaa [72]	2014	children	GA	lower abdominal and perineal surgeries	I	S	dexmedetomidine EA 2 ug/kg	25	1	-	61±26	-
							morphine EA 30 ug/kg	25	4	-	63±24	
Techanivate [73]	2012	-	GA	elective ambulatory gynecologic diagnostic laparoscopy	E	S	dexmedetomidine IV 0.5 ug/kg	20	1	-	35	⑩
							fentanyl IV 0.5 ug/kg	20	5	-	35	
Wan [74]	2011	adults	GA	abdominal surgery, thoracic surgery, lower limb surgery, spine surgery	Po	C	dexmedetomidine IV	102	10	-	-	⑪
							midazolam IV	98	11	-	-	
Nasr [75]	2011	adults	GA	ultra-rapid opiate detoxification	I	C	dexmedetomidine IV	30	0	0	330±18	-
							lefoxidine OR	30	4	1	335±22	
Mountain [76]	2011	children	GA	dental restoration	I	S	dexmedetomidine OR 4 ug/kg	22	0	0	-	-
				and possible tooth extraction			midazolam OR 0.5 ug/kg	19	0	0		
Jung [77]	2011	adults	GA	elective total laparoscopic hysterectomy	E	L	dexmedetomidine IV	25	0	0	98.3±22.5	⑫
							remifentanil IV	25	3	2	97.0±25.3	
Gupta b [78]	2011	adults	SA	lower abdominal surgeries	I	S	dexmedetomidine SA 5 ug	30	1	0	180±45	No
							fentanyl SA 25 ug	30	2	1	170±40	

Bajwa a [80]	2011	adults	EA	vaginal hysterectomies	I	S	dexmedetomidine EA 1.5 ug/kg	25	4	1	96.34±14.58	No
							clonidine EA 2 ug/kg	25	3	1	99.78±13.68	
Bajwa b [79]	2011	adults	EA	lower limb orthopedic surgery	I	S	dexmedetomidine EA 1 ug/kg	50	7	2	102.48±12.36	-
							fentanyl EA 1 ug/kg	50	13	6	108.78±14.49	
Olutoye [81]	2010	children	GA	tonsillectomy and adenoidectomy	I	S	dexmedetomidine IV 0.75 ug/kg	26	2	0	22.0±8.4	-
							dexmedetomidine IV 1 ug/kg	27	0	0	21.3±9.7	
							morphine IV 50 ug/kg	30	0	0	22.8±7.6	
							morphine IV 100 ug/kg	26	3	2	25.9±9.5	
							placebo EA	25	1	-	39±7.6	
Turgut [82]	2009	adults	GA	supratentorial craniotomy	I	L	dexmedetomidine IV	25	3	1	216.08±52.01	-
							remifentanil IV	25	7	3	229.40±37.06	
SaLman [84]	2009	adults	GA	ambulatoty gynecologic laparoscopic surgery	I	L	dexmedetomidine IV	30	-	0	38±22	-
							remifentanil IV	30	-	8	35±22	
Shehabi [83]	2009	adults	GA	pump cardiac surgery	Po	C	dexmedetomidine IV (0.1-0.7) ug/kg/h	152	21	-	-	-
							morphine IV (10-70) ug/kg/h	147	15	-		
Rutkowska [85]	2009	adults	PNB	arteriovenous fistula formation	I	L	dexmedetomidine IV	32	3	-	-	-
							midazolam IV	29	2	-		
Aksu [86]	2009	adults	GA	rhinoplasty	E	S	dexmedetomidine IV 0.5 ug/kg	20	0	0	175.57±53.65	-
							fentanyl IV 1 ug/kg	20	0	1	179.26±64.24	
Turgut [87]	2008	adults	GA	spinal laminectomy	I	L	dexmedetomidine IV	25	8	3	84	-
							fentanyl IV	25	18	12	85	
Kaygusuz [88]	2008	adults	GA	extracorporeal shockwave lithotripsy	I	L	dexmedetomidine IV	20	2	0	37.8±9.2	
							propofol IV	20	5	2	35.5±6.0	
Karaaslan [89]	2007	adults	MAC	septoplasty or endoscopic nasal surgery	I	L	dexmedetomidine IV	35	7	-	28.67±1.27	-
							midazolam IV	35	2	-	30.67±1.33	
Demiraran [90]	2007	adults	GA	esophagogastroduodenal endoscopy	I	L	dexmedetomidine IV	25	1	0	8.9±1.3	-
							midazolam IV	25	2	2	9,03±1.2	
Bulow [91]	2007	adults	GA	gynecologic videolaparoscopic surgery	I	C	dexmedetomidine IV 0.5 ug/kg	15	4	-	118.7±13.4	-
							remifentanil IV 0.3 ug/kg	15	2	-	92.9±8.0	
Kanazi [92]	2006	adults	SA	transurethral resection of prostate or bladder tumor	I	S	dexmedetomidine SA 3 ug	16	0	0	56±18	-
							clonidine SA 30 ug	16	0	0	77±48	
Jalowiecki [93]	2005	adults	GA	ambulatory elective colonoscopy	I	L	dexmedetomidine IV	19	5	-	-	-
							fentanyl IV	24	0	-		
Herr [94]	2003	adults	-	coronary artery bypass graft surgery	Po	L	dexmedetomidine IV	148	22	-	-	-
							propofol IV	147	19	-		
Chaves [95]	2003	adults	GA	videolaparoscopic cholecystectomy	I	L	dexmedetomidine IV	21	9	-	-	-

				remifentanil IV	21	6 -

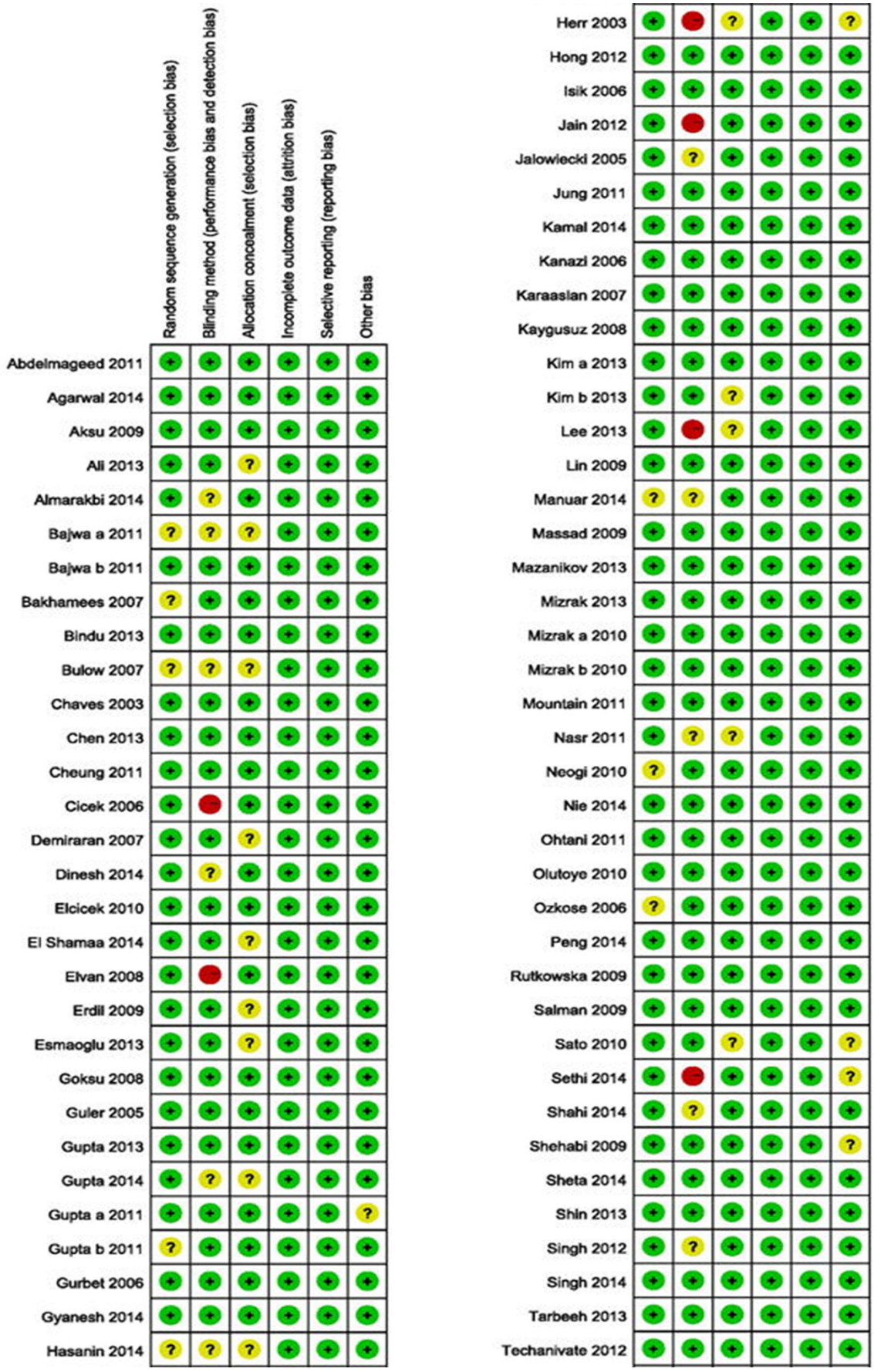
GA: general anesthesia, SA: spinal anesthesia, EA: epidural anesthesia, PNB: peripheral neural blockade, IVRA: intravenous regional anesthesia, MAC: monitored anesthesia care, IV: intravenous, IA: intraarticular, OR: oral, IN: intranasal, I: induction of anesthesia, E: end of surgery, Po: postoperative, S: single dose, L: loading dose followed by continuous infusion, C: continuous infusion. ① National Natural Science Foundation of China (81000824). ② Science and Technology Program of Guangdong Province, Research Project of Commission on Innovation and Technology of Guangzhou (2011KP304), Youth Foundation of The Third Affiliated Hospital of Guangzhou Medical University (2010Y05). ③ Supported by themselves and institution. ④ Supported by Wonkwang University. ⑤ Medical and Health Foundation of Guangzhou City (201102A213071). ⑥ Supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan to N.O. (No. 21791429) and E.M. (No. 22659362). ⑦ Supported in part by the University of Hong Kong CRCG Small Project Fund (200807176008). ⑧ Supported in part by Grants-in-Aid for Scientific Research from the Japanese Ministry of Education, Science, Sports, and Culture (No. 17591627). ⑨ Supported in part by an unrestricted educational grant from Hospira, Inc. (Lake Forest, IL), endowment funds from the Margaret Milam McDermott Distinguished Chair in Anesthesiology, and the White Mountain Institute, a non-profit private foundation (Paul F. White, President). ⑩ Rachadapisek Sompoch Fund of Chulalongkorn University, Bangkok, Thailand (RA 57/53). ⑪ National Natural Science Foundation of China (81060033). ⑫ 2010 Research Fund from the Research Institute of Medical Science, St Vincent's Hospital, Suwon, Republic of Korea.

Table 2. Efficacy of intravenous dexmedetomidine on reducing nausea and vomiting compared with placebo

Comparison	Number of studies	dexme-detomidine	placebo	RR (95% CI)	I^2	References
Nausea						
Investigator initiated trail/dosage regimen/dose						
Induce	26	101/783	172/776	0.59 (0.48, 0.73)	20%	[14, 18, 19, 24-30, 37, 39, 41, 46, 47, 49, 51-55, 57-61]
End	5	11/160	28/157	0.38 (0.21, 0.69)	0%	[17, 22, 35, 42, 50]
Single dose	15	50/447	79/444	0.63 (0.47, 0.86)	0%	[14, 17, 20, 22, 24, 25, 28, 35, 37, 41, 45, 46, 50, 56, 58, 61]
Loading dose followed by continuous infusion	13	42/381	93/383	0.46 (0.34 0.62)	24%	[19, 26, 27, 30, 42, 47, 52-55, 57, 59, 60]
0.5 μg/kg	6	26/181	39/179	0.67 (0.45, 0.99)	0%	[17, 25, 28, 45, 46, 50]
1.0 μg/kg	8	24/236	36/235	0.67 (0.41, 1.07)	5%	[22, 24, 35, 37, 41, 56, 58, 61]
Vomiting						
Investigator initiated trails/dosage regimen/dose						
Induce	13	29/389	63/388	0.45 (0.31, 0.67)	0%	[24, 25, 29, 32, 43, 47-49, 51, 52, 55, 60, 61]
End	7	18/235	29/233	0.62 (0.38, 1.02)	0%	[17, 22, 33-35, 50, 62]
single dose	14	25/425	42/426	0.60 (0.39, 0.92)	0%	[17, 22, 24, 25, 33-35, 43, 45, 48, 50, 56, 61, 62]
loading dose followed by continuous infusion	5	11/152	30/151	0.36 (0.19, 0.67)	0%	[32, 47, 52, 55, 60]
0.5 μg/kg	6	12/165	17/163	0.71 (0.40, 1.25)	0%	[17, 25, 45, 48, 50, 62]
1.0 μg/kg	5	5/156	17/156	0.29 (0.12, 0.75)	0%	[22, 24, 35, 56, 61]

Table 3. Efficacy of dexmedetomidine on reducing nausea and vomiting with high risk factors compared with placebo

Comparison	Number of studies	dexmedetomidine	placebo	RR (95% CI)	I^2	References
Nausea						
Female sex	11	51/348	85/344	0.59 (0.44, 0.79)	0%	[17, 20, 22, 24, 27-29, 39, 49, 53, 59]
Laparoscopy	6	19/220	46/218	0.40 (0.25, 0.66)	0%	[22, 27, 35, 46, 49, 55]
Postoperative opioid treatment	9	40/233	79/233	0.50 (0.37, 0.69)	22%	[27, 29, 38, 42, 51, 55, 59-61]
Vomiting						
Female sex	5	14/168	30/163	0.30 (0.13, 0.66)	0%	[17, 22, 24, 29, 49]
Laparoscopy	5	8/182	19/179	0.36 (0.15, 0.87)	0%	[22, 35, 49, 51, 55]
Postoperative opioid treatment	7	14/185	34/185	0.42 (0.25, 0.70)	0%	[29, 33, 38, 51, 55, 60, 61]


Random sequence generation (selection bias)
Blinding method (performance bias and detection bias)
Allocation concealment (selection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Abdelmageed 2011
Agarwal 2014
Aksu 2009
Ali 2013
Almarakbi 2014
Bajwa a 2011
Bajwa b 2011
Bakhamees 2007
Bindu 2013
Bulow 2007
Chaves 2003
Chen 2013
Cheung 2011
Cicek 2006
Demiraran 2007
Dinesh 2014
Elcicek 2010
El Shamaa 2014
Elvan 2008
Erdil 2009
Esmaoglu 2013
Goksu 2008
Guler 2005
Gupta 2013
Gupta 2014
Gupta a 2011
Gupta b 2011
Gurbet 2006
Gyanesh 2014
Hasanin 2014
Herr 2003
Hong 2012
Isik 2006
Jain 2012
Jalowiecki 2005
Jung 2011
Kamal 2014
Kanazi 2006
Karaaslan 2007
Kaygusuz 2008
Kim a 2013
Kim b 2013
Lee 2013
Lin 2009
Manuar 2014
Massad 2009
Mazanikov 2013
Mizrak 2013
Mizrak a 2010
Mizrak b 2010
Mountain 2011
Nasr 2011
Neogi 2010
Nie 2014
Ohtani 2011
Olutoye 2010
Ozkose 2006
Peng 2014
Rutkowska 2009
Salman 2009
Sato 2010
Sethi 2014
Shahi 2014
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Singh 2012
Singh 2014
Tarbeeh 2013
Techanivate 2012

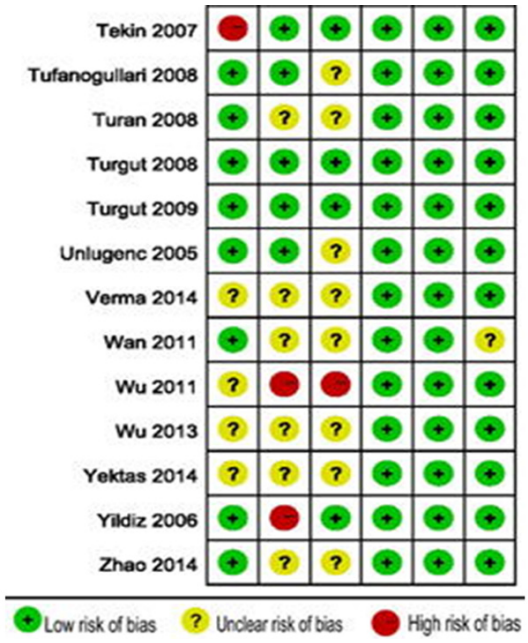

Figure 2. Summary of the risk of bias of the included studies.

midine with placebo. The incidence of nausea (pooled RR = 0.61, 95% CI: 0.50 to 0.73) and vomiting (pooled RR = 0.48, 95% CI: 0.36 to 0.64) in the dexmedetomidine group was significantly lower than the placebo group (**Figures 3**, **4**). Begg's Test suggested that no significant publication bias existed in the comparisons of nausea (P = 0.957) and vomiting (P = 0.488) between dexmedetomidine and placebo.

Further, factors that affected nausea and vomiting were evaluated through subgroup analysis.

Type of anesthesia: Dexmedetomidine significantly reduced the incidence of both nausea (pooled RR of 27 trails [14, 18, 22, 24-30, 35, 38, 39, 41, 42, 46, 49-51, 53, 55-61]: 0.57, 95% CI: 0.46 to 0.69) and vomiting (pooled RR of 20 trails [21, 22, 24, 25, 29, 32-35, 38, 43, 48-51, 55, 56, 60-62]: 0.50, 95% CI: 0.37 to 0.68) after general anesthesia, but not regional anesthesia (nausea: pooled RR of 16 trials [15-17, 19-21, 23, 31, 36, 37, 40, 44, 45, 47, 52, 54]: 0.78, 95% CI: 0.51 to 1.19; vomiting: pooled RR of seven trails [17, 23, 31, 40, 45, 47, 52]: 0.30, 95% CI: 0.11 to 0.85) (**Figures 3**, **4**).

Route of administration: Dexmedetomidine injected intravenously lowered the incidence of nausea (pooled RR of 34 trails [14, 17-19, 22, 24-30, 35, 37-39, 41, 42, 45-47, 49-61]: 0.55, 95% CI: 0.45 to 0.67) and vomiting (pooled RR of 23 trails [17, 22, 24, 25, 29, 32-35, 38, 43, 45, 47-52, 55, 56, 60-62]: 0.47, 95% CI: 0.35 to 0.63), but not epidurally (nausea: pooled RR of three trails [16, 32, 36, 44]: 1.80, 95% CI: 0.64 to 5.07; vomiting: none) or intrathecally (nausea: pooled RR of four trials [15, 23, 31, 40]: 1.73, 95% CI: 0.63 to 4.71; vomiting: pooled RR of three trails [23, 31, 40]: 1.00, 95% CI: 0.07 to 15.26) (**Figures 5**, **6**).

Administration of IV dexmedetomidine: Subgroup analysis not only demonstrated single dose (nausea: pooled RR of 15 trails [14, 17, 20, 22, 24, 25, 28, 35, 37, 41, 45, 46, 50, 56, 58, 61]: 0.63, 95% CI: 0.47 to 0.86; vomiting: pooled RR of 14 trails [24, 25, 29, 32, 43, 47-49, 51, 52, 55, 60, 61]: 0.60, 95% CI: 0.39 to 0.92), loading dose followed by continuous infusion (nausea: pooled RR of 13 trails [19, 26, 27, 30, 42, 47, 52-55, 57, 59, 60]: 0.46, 95% CI: 0.34 to 0.62; vomiting: pooled RR of five trails [32, 47, 52, 55, 60]: 0.36, 95% CI: 0.19 to 0.67) of dexmedetomidine could reduce the incidence of nausea and vomiting with any investigator initiated trails, induce of anesthesia (nausea: pooled RR of 26 trails [14, 17, 20, 22, 24, 25, 28, 35, 37, 41, 45, 46, 50, 56, 58, 61]: 0.59, 95% CI: 0.48 to 0.73; vomiting: pooled RR of 13 trails [24, 25, 29, 32, 43, 47-49, 51, 52, 55, 60, 61]: 0.45, 95% CI: 0.31 to 0.67) and end of surgery (nausea: pooled RR of five trails [17, 22, 35, 42, 50]: 0.38, 95% CI: 0.21 to 0.69; vomiting: pooled RR of seven trails [17, 22, 33-35, 50, 62]: 0.62, 95% CI: 0.38 to 1.02), but also suggested a beneficial effect of a single-dose bolus of 0.5 μg/kg dexmedetomidine compared with placebo on nausea (pooled RR of six trials [17, 25, 28, 45, 46, 50]: 0.46, 95% CI: 0.34 to 0.62), while 1.0 μg/kg dexmedetomidine reduced the incidence of vomiting (pooled RR of five trials [22, 24, 35, 56, 61]: 0.29, 95% CI: 0.12 to 0.75) (**Table 2**).

Efficacy on PONV with high risk factors: Subgroup analysis suggested a significant efficacy of dexmedetomidine on nausea and vomiting with high risk factors, like female sex (nausea: pooled RR of 11 trials [17, 20, 22, 24, 27-29, 39, 49, 53, 59]: 0.59, 95% CI: 0.44 to 0.79; vomiting: pooled RR of five trials [17, 22,

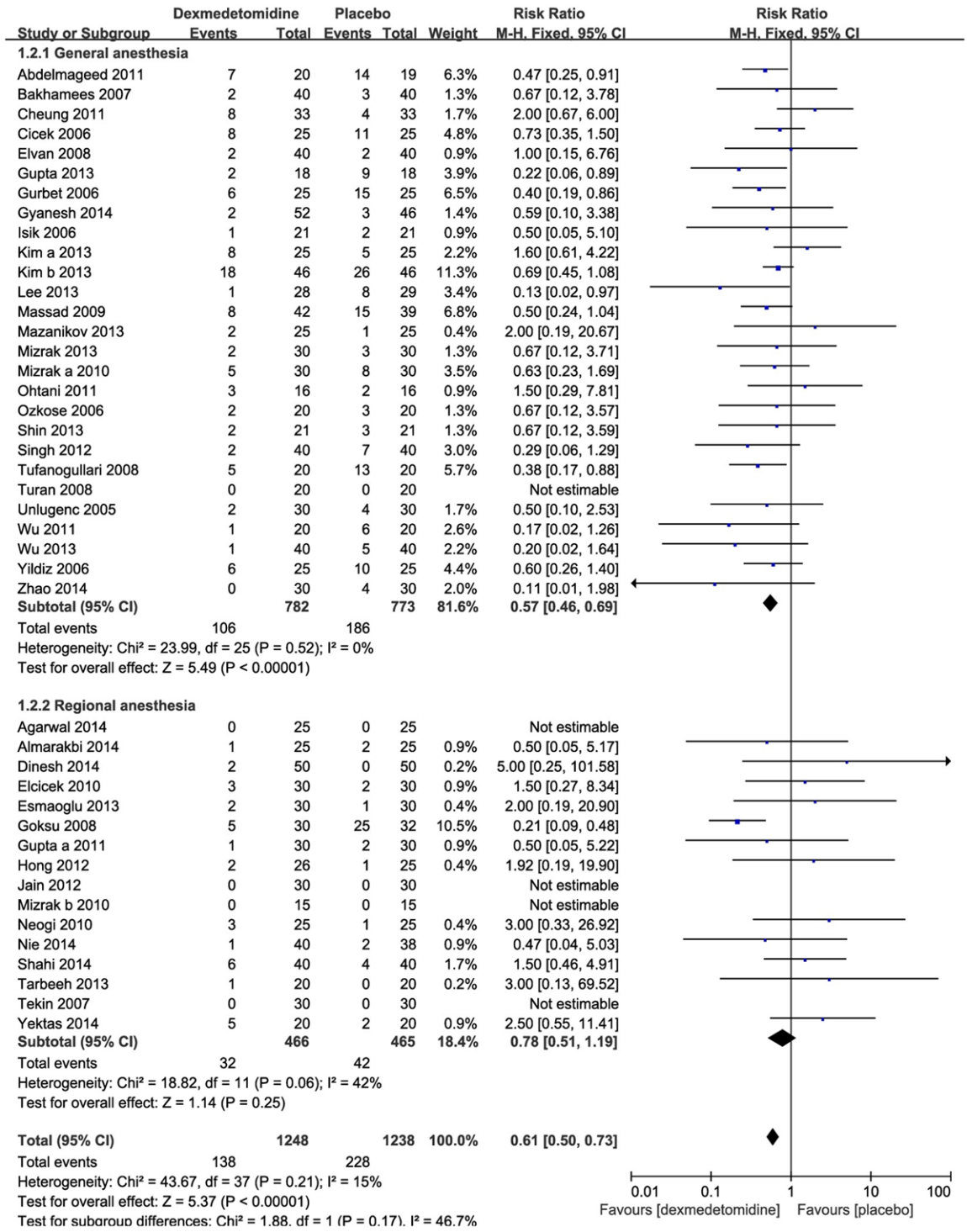

Figure 3. Results of subgroup analysis of the incidence of postoperative nausea by anesthesia types.

24, 29, 49]: 0.30, 95% CI: 0.13 to 0.66), laparoscopy (nausea: pooled RR of six trials [22, 27, 35, 46, 49, 55]: 0.40, 95% CI: 0.25 to 0.66; vomiting [22, 35, 49, 51, 55]: pooled RR of five trials: 0.36, 95% CI: 0.15 to 0.87), postoperative opioid treatment (nausea: pooled RR of nine trials [27, 29, 38, 42, 51, 55, 59-61]: 0.50, 95% CI: 0.37 to 0.69; vomiting: pooled RR of five trials [29, 33, 38, 51, 55, 60, 61]: 0.42, 95% CI: 0.25 to 0.70) (**Table 3**).

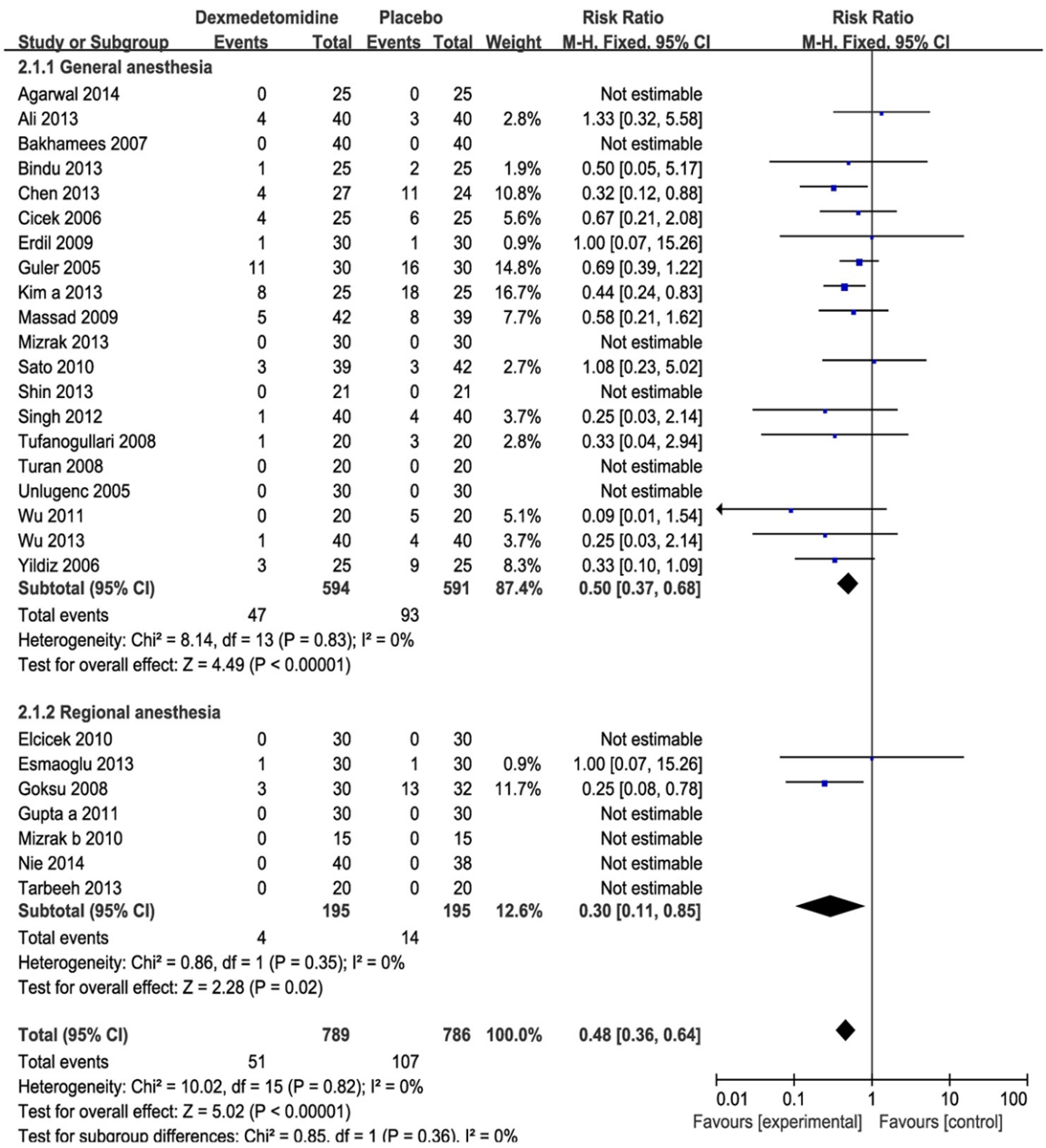

Figure 4. Results of subgroup analysis of the incidence of postoperative vomiting by anesthesia types.

Consumption of intraoperative analgesics: Application of dexmedetomidine reduced the dose of intraoperative fentanyl infused as the only analgesic agent intravenously (pooled SMD of five trails [24, 30, 38, 49, 55, 59]: -1.91, 95% CI: -3.20 to -0.62) compared with placebo. A sensitivity analysis to remove a high-risk study [38] showed a similar result favoring dexmedetomidine (pooled SMD = -2.30, 95% CI: -3.86 to -0.73), but still did not decrease heterogeneity (I^2 = 95%) (**Figure 7**).

Dexmedetomidine vs. other agents: Forty-one studies [16, 18, 23, 32, 34, 44, 46, 48, 63-77, 79-96], compared the efficacy of dexmedetomidine with other drugs on nausea and vomiting, involving 2,536 and 1,368 patients in each group. Dexmedetomidine could reduce the incidence of vomiting compared with the total agents (pooled RR of 24 trials [23, 32, 34, 35, 48, 63, 66, 68-70, 75-77, 79-82, 84, 86-88, 90, 92, 96]: 0.28, 95% CI: 0.18 to 0.43), but not nausea (pooled RR of 34 trials [16, 18, 23,

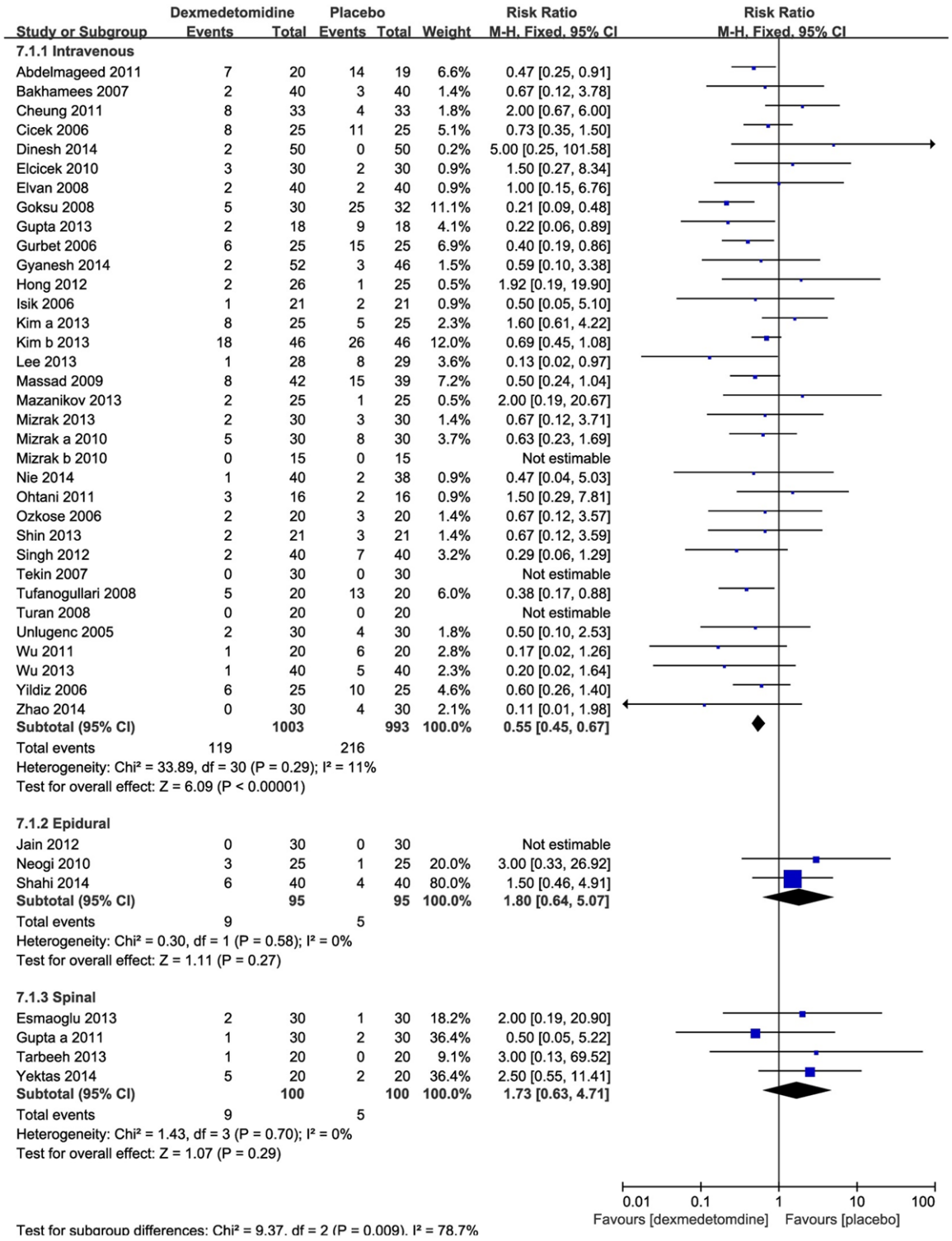

Figure 5. Results of subgroup analysis of the incidence of postoperative nausea by routes of dexmedetomidine administration.

44, 46, 63, 65, 67-69, 71-77, 79-83, 85-96]: 0.89, 95% CI: 0.73 to 1.09). Further, the significant difference could be found specifically between dexmedetomidine and opioids (nausea: pooled RR of 16 trials [23, 68, 69, 72, 73, 77, 80-83, 86, 87, 91, 93, 95, 96]: 0.75, 95% CI:

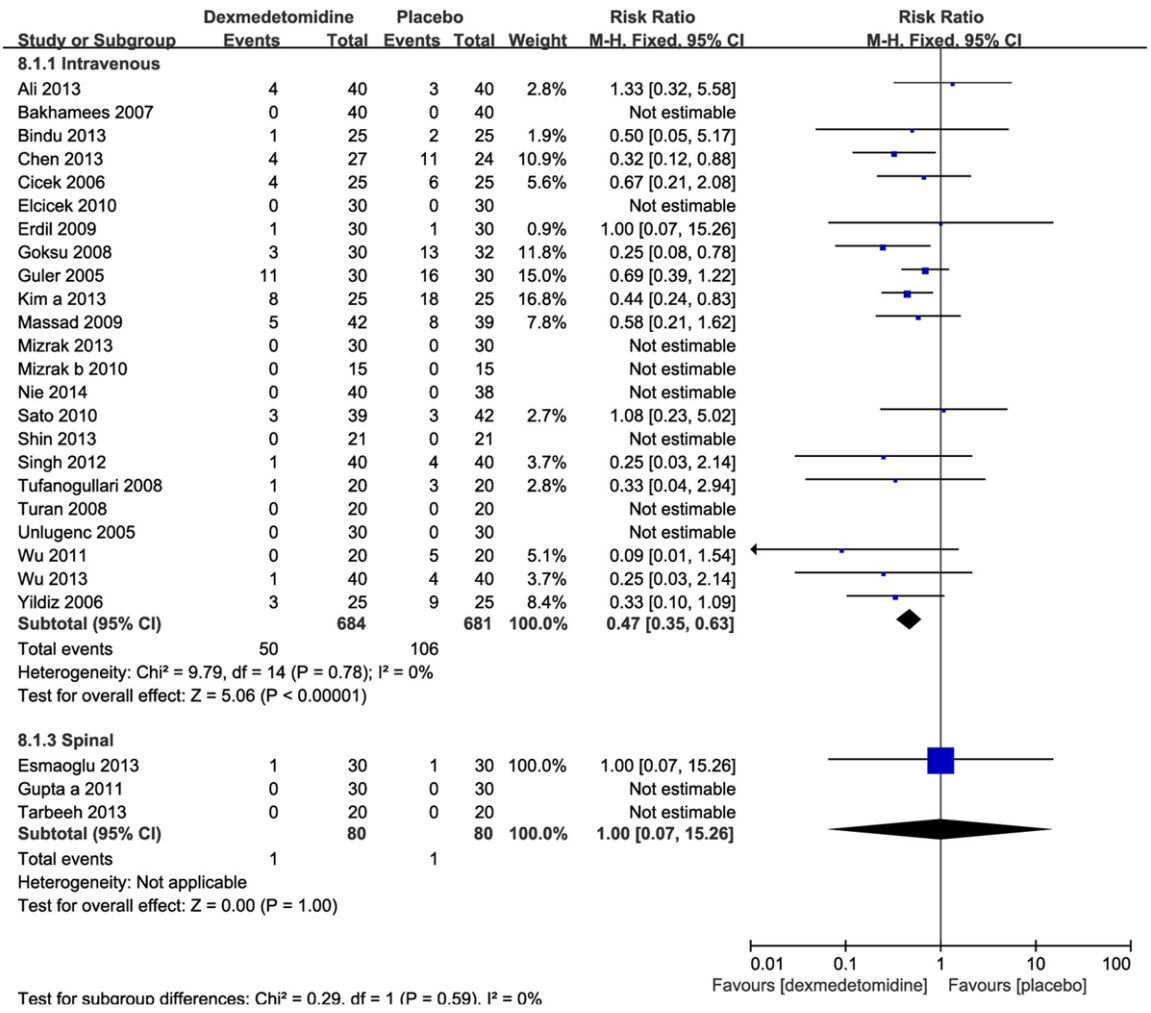

Figure 6. Results of subgroup analysis of the incidence of postoperative vomiting by routes of dexmedetomidine administration.

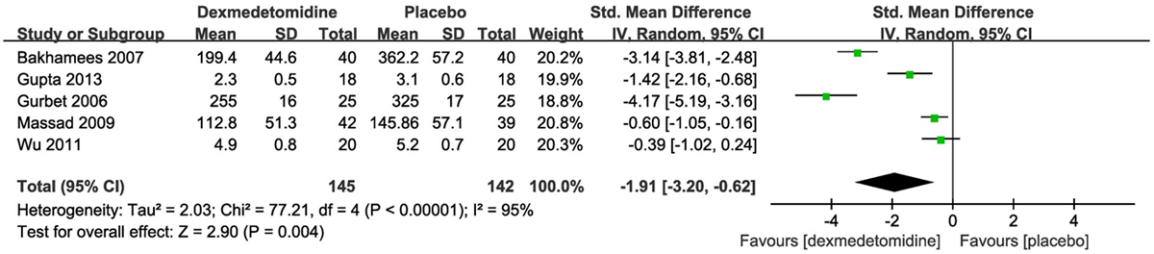

Figure 7. Consumption of intraoperative fentanyl with the application of dexmedetomidine.

0.56 to 0.99; vomiting: pooled RR of 12 trials [23, 48, 68, 69, 77, 80-82, 84, 86, 87, 96]: 0.22, 95% CI: 0.12 to 0.41), but not sedation agents (nausea: pooled RR of ten trials [63, 65, 67, 74, 76, 85, 88-90, 94]: 1.08, 95% CI: 0.75 to 1.54; vomiting: pooled RR of seven trials [34, 63, 66, 70, 76, 88, 90]: 0.57, 95% CI: 0.26 to 1.23) (**Table 4**).

Sensitivity analysis: Upon the studies with high risk were excluded by sensitivity analysis, there was no significant difference in results from overall pooled estimates across all outcomes above.

Table 4. Efficacy of dexmedetomidine on reducing nausea and vomiting compared with other agents

Comparison	Number of studies	dexmedetomi-dine	agents	RR (95% CI)	I^2	References
nausea	34	145/1275	162/1261	0.89 (0.73, 1.09)	20%	[16, 18, 23, 44, 46, 63, 65, 67-69, 71-77, 79-83, 85-96]
opioids	16	66/537	89/536	0.75 (0.56, 0.99)	40%	[23, 68, 69, 72, 73, 77, 80-83, 86, 87, 91, 93, 95, 96]
fentanyl	8	23/217	39/222	0.61 (0.40, 0.94)	29%	[23, 68, 73, 80, 86, 87, 93, 96]
remifentanil	4	16/86	18/86	0.89 (0.50, 1.60)	45%	[77, 82, 91, 95]
morphine	4	27/234	32/228	0.83 (0.52, 1.33)	51%	[69, 72, 81, 83]
sedation agents	10	55/490	50/477	1.08 (0.75, 1.54)	0%	[63, 65, 67, 74, 76, 85, 88-90, 94]
propofol	4	28/238	28/235	0.99 (0.61, 1.61)	0%	[63, 67, 88, 94]
midazolam	6	27/252	22/242	1.19 (0.70, 2.03)	0%	[65, 74, 76, 85], 86], 89], 90]
vomiting	24	23/687	82/681	0.28 (0.18, 0.43)	0%	[23, 32, 34, 35, 48, 63, 66, 68-70, 75-77, 79-82, 84, 86-88, 90], 92], 96]
opioids	12	11/340	48/339	0.27 (0.15, 0.47)	0%	[23, 48, 68, 69, 77, 80-82, 84, 86, 87, 96]
fentanyl	7	7/203	25/203	0.25 (0.11, 0.59)	0%	[23, 48, 68, 80, 86, 87, 96]
remifentanil	3	1/80	13/80	0.12 (0.03, 0.55)	0%	[77, 82, 84]
morphine	2	3/57	10/56	0.27 (0.07, 1.00)	0%	[69, 81]
sedation agents	7	8/216	15/211	0.57 (0.26, 1.23)	0%	[34, 63, 66, 70, 76, 88, 90]
propofol	4	6/139	9/137	0.67 (0.25, 1.84)	0%	[34, 63, 70, 88]
midazolam	3	2/77	6/74	0.35 (0.08, 1.61)	0%	[66, 76, 90]

Discussion

PONV is a long-standing problem, not a new concept in anesthesiology. Despite plenty of studies over the past few decades, PONV remains an extremely significant challenge due to its complex mechanism, resulting in serious consequences. Therefore an effective way to prevent or arrest PONV is urgently needed as ever.

The present meta-analysis was undertaken to evaluate the efficacy of dexmedetomidine on the prevention of nausea and vomiting. The main findings are as follows: (1) Dexmedetomidine shows superiority to placebo, in the prevention of nausea and vomiting with high-risk factors or not, and opioids, but not to sedation agents. (2) The beneficial effect of dexmedetomidine on nausea and vomiting can be achieved through intravenous injection only, with common timing of administration and dosage regimen. (3) As the most commonly used dose in published articles, intravenous 0.5 μg/kg bolus infusion has a preventive effect on nausea, while 1.0 μg/kg bolus infusion reduces the indication of vomiting. (4) Using of dexmedetomidine reduces the total intraoperative consumption of analgesic agents.

This beneficial antiemetic effect may be explained by direct antiemetic properties of α_2 agonists, although the biologic basis remains obscure. Additionally, since nausea and vomiting may be induced by high catecholamine concentrations, a decrease of sympathetic tone could explain the antiemetic effect of dexmedetomidine. Finally, consumption of intraoperative opioids, which increases the risk of PONV [97], may be reduced through the use of dexmedetomidine.

Controversy existed in previous meta-analysis about the efficacy on nausea and vomiting, several studies [22, 98, 99] suggested an absolutely superior role of dexmedetomidine compared with placebo, but the others [100-102] not. However, only analyzing nine trails at most, these results might be equivocal relatively. And dexmedetomidine was also not compared with other agents directly. In contrast, we included 82 articles with vast clinical outcome variables to improve the reliability of our conclusion.

To the best of our knowledge, this is the first time to shed light on the efficacy of dexmedetomidine on nausea and vomiting from a variety of aspects, by a meta-analysis of RCTs. The majority of included trials were well designed and assessed as “Low”. Moreover, we directly compared dexmedetomidine with opioid analgesics and sedation agents, meanwhile eliminated studies with high risk by sensitivity analysis. All of these strategies were administrated to come up with a solid conclusion.

The clinical usage of dexmedetomidine to prevent nausea and vomiting is still unascertained. So in this meta-analysis, we newly found that 0.5 μg/kg bolus infusion was sufficiently effective to prevent nausea, and 1.0 μg/kg dexmedetomidine only reduces the occurrence of vomiting, interestingly. Our result that only intravenous dexmedetomidine, not epidural or spinal, was an available option for antiemetic might cause confusion, since regional administration has always been used widely as a fast and cheap way. We speculate that high hydrophobic may be responsible. Dexmedetomidine might decrease the noradrenergic activity as a result of binding to α_2 presynaptic inhibitory adrenoreceptor in the locus coeruleus, an inhibition that probably resulted in an antiemetic effect [103]. But only about 22% of the epidural dose was identified in cerebrospinal fluid, the other dose was distributed into epidural fat. And as a highly hydrophobic agent, dexmedetomidine could non-specifically bind to spinal cord white matter that limited dexmedetomidine to transferring towards the pontine brain stem [104], which possibly cut off potential antiemetic pathway mentioned above. Therefore, even extradural 1-2 μg/kg or subarachnoid 3-5 μg dexmedetomidine mentioned in the included trials may not be enough to reach the plasma concentration activating the receptors which may inhibit PONV compared with at least 0.3 μg/kg intravenously.

Still, this meta-analysis has several limitations. First, the total number of trails included is significant relatively, but the amounts in some subgroups, like dose, epidural or spinal infuse, consumption of intraoperative fentanyl subgroups etc., is still too little to secure the conclusive results. Second, only 32 trials reported the source of their funding, however we did not know whether or not the others were supported by companies or industries, which may incline the design towards the best light of drug. Third, the high risk factors of PONV, like prior history

of motion sickness and/or PONV and nonsmoker, were so difficult to detect throughout the literature that we failed to include these as the evaluation items. Forth, the significant heterogeneity in analgesic consumption subgroup, due to the different types and lengths of surgeries probably, still exists after lots of efforts. Therefore, more RCTs, including kinds of patients and various doses or routes of administration in specific surgeries or anesthesia, should be designed reasonably to detect the efficacy of dexmedetomidine on PONV.

In conclusion, our present meta-analysis demonstrated that the intravenous infusion of dexmedetomidine may reduce the incidence of PONV, compared with placebo and opioids, rather than sedatives, which is due to the reduced consumption of intraoperative opioids probably. The results may provide a new evidence to expand the clinical value of dexmedetomidine in addition to its routine usage for analgesia and sedation.

Acknowledgements

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Disclosure of conflict of interest

None.

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