三联方案防治中高度致吐风险化疗药物致急性恶心呕吐疗效的网状Meta分析Δ

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摘　要　目的　评价5-羟色胺3（5-HT$_3$）受体拮抗剂、神经激肽-1（NK-1）受体拮抗剂和地塞米松联用方案（以下简称“三联方案”）防治中高度致吐风险化疗药物致急性恶心呕吐的疗效。**方法**　检索PubMed、Embase、Cochrane图书馆、中国期刊全文数据库、万方数据，收集不同三联方案或5-HT$_3$受体拮抗剂联用地塞米松（以下简称“二联方案”）的随机对照试验（RCT），检索时限为建库至2023年5月。筛选文献、提取资料、评价文献质量后，采用Stata 16.0软件进行网状Meta分析。**结果**　共纳入59项RCT，共计23 418例患者，涉及15种干预措施。网状Meta分析结果显示，急性恶心呕吐控制率方面，以福沙匹坦+帕洛诺司琼+地塞米松（FPD）疗效最优，其次为福沙匹坦+格拉司琼+地塞米松（FGD）和阿瑞匹坦+雷莫司琼+地塞米松（AMD）；急性恶心控制率方面，以FPD的疗效最优，其次为阿瑞匹坦+帕洛诺司琼+地塞米松（APD）和FGD；急性呕吐控制率方面，以FPD疗效最优，其次为FGD和APD。**结论**　福沙匹坦+格拉司琼+地塞米松较其他三联方案或二联方案防治中高度致吐风险化疗药物所致急性恶心呕吐的疗效更好。
关键词　5-羟色胺3受体拮抗剂；神经激肽-1受体拮抗剂；地塞米松；恶心呕吐；网状Meta分析

Network meta-analysis of triple therapy for the prevention and treatment of acute nausea and vomiting caused by emetogenic chemotherapy drugs with moderate and high risk

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ABSTRACT　OBJECTIVE To evaluate the efficacy of the triple therapy of 5-HT$_3$ receptor antagonists，neurokinin-1 receptor antagonists and dexamethasone（referred to as “triple therapy”）in the prevention and treatment of acute nausea and vomiting caused by moderately and highly emetogenic chemotherapy drugs. **METHODS** Retrieved from PubMed，Embase，the Cochrane Library，CNKI and Wanfang data，randomized controlled trials（RCTs）about triple therapy or 5-HT$_3$ receptor antagonist combined with dexamethasone（referred to as “dual therapy”）were collected during the inception to May 2023. After literature screening，data extraction and literature evaluation，network meta-analysis was performed by using Stata 16.0 software. **RESULTS** A total of 59 RCTs were included，involving 23 418 patients and 15 interventions. Results of network meta-analysis showed that fosaprepitant + palonosetron + dexamethasone（FPD）was most effective in terms of acute nausea and vomiting control rate，followed by fosaprepitant + granisetron + dexamethasone（FGD）and aprepitant + ramosetron + dexamethasone（AMD）. In terms of acute nausea control rate，FPD was the most effective，followed by aprepitant + palonosetron + dexamethasone（APD）and FGD. In terms of acute vomiting control rate，FPD was the most effective，followed by FGD and APD. **CONCLUSIONS** Fosaprepitant + palonosetron + dexamethasone is better than other triple therapy or dual therapy in preventing acute nausea and vomiting caused by moderately and highly emetogenic chemotherapy drugs.
KEYWORDS　5-HT$_3$ receptor antagonist；neurokinin-1 receptor antagonist；dexamethasone；nausea and vomiting；network meta-analysis

化疗药物导致的恶心呕吐（chemotherapy-induced nausea and vomiting，CINV）是肿瘤治疗过程中最常见的不良反应之一，严重影响患者的食欲或进食过程。CINV可引起患者代谢异常，加重其营养不良，最终影响患者的生存质量、用药依从性及预后[1]。因此，有效地预防和治疗CINV是肿瘤治疗顺利进行的保障。目前，临床常用的止吐药物按其作用机制分为5-羟色胺3（5-hydroxytryptamine 3，5-HT$_3$）受体拮抗剂、神经激肽-1（neurokinin-1，NK-1）受体拮抗剂和糖皮质激素等。《中国肿

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瘤药物治疗相关恶心呕吐防治专家共识（2022年版）》推荐，在高度致吐风险化疗药物使用前，可采用5-HT_3受体拮抗剂、NK-1受体拮抗剂和地塞米松联用方案（以下简称“三联方案”）来预防CINV（2A，Ⅰ类证据），对于既往治疗失败的中度CINV的预防也应使用三联方案[1]。目前，虽然已有临床试验评价了三联方案的治疗效果，但未对其进行整体评估和优劣分析。网状Meta分析可通过间接比较得到任意两种治疗方案的优劣结果，同时对不同干预措施进行排序，对指导临床医师开展用药具有一定意义。本研究采用网状Meta分析的方法评价了不同三联方案防治中高度致吐风险化疗药物致急性CINV的疗效，旨在为临床用药提供参考。

1 资料与方法

1.1 纳入与排除标准

1.1.1 研究类型

本研究纳入的文献类型为随机对照试验（randomized controlled trial，RCT）。语种为中、英文。

1.1.2 研究对象

本研究纳入的患者均经病理组织学或细胞学检查确诊为恶性肿瘤，肿瘤类型不限。

1.1.3 干预措施

观察组患者的干预措施均为不同的三联方案，对照组患者的干预措施均为不同的三联方案或5-HT_3受体拮抗剂联用地塞米松（以下简称“二联方案”）。5-HT_3受体拮抗剂包括昂丹司琼、格拉司琼等；NK-1受体拮抗剂包括阿瑞匹坦、福沙匹坦等。

1.1.4 结局指标

本研究的结局指标包括：急性恶心控制率、急性呕吐控制率和急性CINV控制率。

1.1.5 排除标准

本研究的排除标准包括：（1）正在进行或尚未发布研究结果的文献；（2）缺少结局指标、研究数据不全或无法获取原文的文献；（3）重复发表的文献。

1.2 文献检索策略

检索PubMed、Embase、Cochrane图书馆、中国期刊全文数据库、万方数据。中文检索词为“恶心”“呕吐”“5-HT_3受体拮抗剂”“昂丹司琼”“格拉司琼”“托烷司琼”“帕洛诺司琼”“雷莫司琼”“NK-1受体拮抗剂”“阿瑞匹坦”“福沙匹坦”“奈妥匹坦”“卡索匹坦”“罗拉匹坦”“止吐方案”；英文检索词为“nausea”“vomiting”“5-HT_3 receptor antagonists”“ondansetron”“granisetron”“tropisetron”“palonosetron”“ramosetron”“neurokinin-1 inhibitors”“aprepitant”“fosaprepitant”“netupitant”“casopitant”“rolapitant”“antiemetic regimens”。检索时间为建库起至2023年5月。

1.3 文献筛选与资料提取

由2位研究者独立完成，排除明显不符合纳入标准的研究并交叉核对，如有分歧，请第3位研究者共同商议。提取资料包括第一作者、发表年份、国家、化疗强度、干预措施、结局指标等。

1.4 纳入文献质量评价

按照Cochrane系统评价员手册5.1.0推荐的风险评价工具进行质量评价，具体包括：随机分配方法、分配隐藏、盲法实施、结局数据完整性、选择性报告结果、偏倚来源，每项分为“低风险”“高风险”“不清楚”[2]。

1.5 统计学分析

利用Stata 16.0软件进行网状Meta分析，并绘制证据关系图。数据以比值比（odds ratio，OR）及其95%置信区间（confidence interval，CI）表示。采用I^2检验分析统计学异质性，若$P>0.10$，$I^2\leqslant 50\%$，采用固定效应模型；反之，采用随机效应模型。当存在闭环时，通过节点劈裂法检验是否存在不一致性，$P>0.05$为一致性良好，采用一致性模型分析；反之，采用不一致性模型分析。根据累积排序曲线下面积（surface under cumulative ranking curve，SUCRA）对疗效优劣进行排序，SUCRA越大，表示疗效越好[3]。采用倒漏斗图进行发表偏倚分析。检验水准$\alpha=0.05$。

2 结果

2.1 文献筛选结果和纳入研究基本特征

初检获得相关文献11 909篇，经阅读题目、摘要及全文后，最终纳入59篇文献[4—62]，共计23 418例患者；共涉及15种干预措施，分别为阿瑞匹坦+格拉司琼+地塞米松（AGD）、阿瑞匹坦+昂丹司琼+地塞米松（AOD）、阿瑞匹坦+帕洛诺司琼+地塞米松（APD）、阿瑞匹坦+托烷司琼+地塞米松（ATD）、福沙匹坦+格拉司琼+地塞米松（FGD）、奈妥匹坦+帕洛诺司琼+地塞米松（NPD）、罗拉匹坦+格拉司琼+地塞米松（UGD）、卡索匹坦+昂丹司琼+地塞米松（KOD）、阿瑞匹坦+雷莫司琼+地塞米松（AMD）、福沙匹坦+昂丹司琼+地塞米松（FOD）、福沙匹坦+帕洛诺司琼+地塞米松（FPD）、格拉司琼+地塞米松（GD）、托烷司琼+地塞米松（TD）、帕洛诺司琼+地塞米松（PD）、昂丹司琼+地塞米松（OD）。结果见图1、表1。

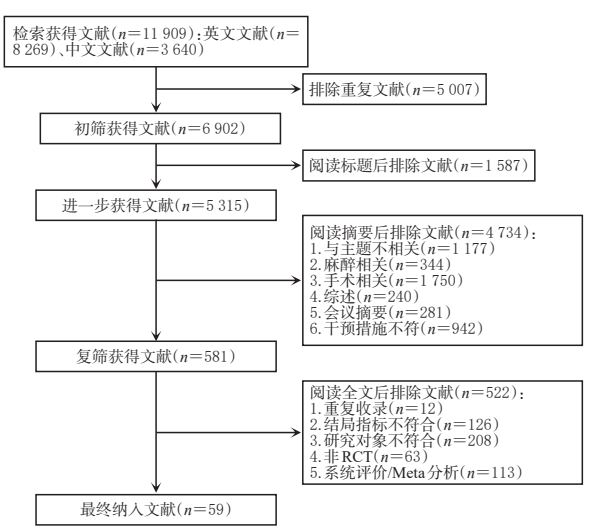

图1 文献筛选流程图

表1　纳入研究的基本特征

第一作者及发表年份	例数		年龄/岁		干预措施		化疗药物致吐风险强度	结局指标
	观察组	对照组	观察组	对照组	观察组	对照组		
Li 2019[4]	50	50	51.7±7.1	47.8±8.2	ATD	TD	高	①
Kim 2015[5]	144	155	58.9±10.4	59.0±11.6	AMD	AOD	高	①
Kang 2020[6]	137	142	59.4±12.0	60.3±11.8	AMD	APD	高	①
黄韬2020[7]	99	98	38.6±4.2	38.8±4.7	APD	PD	高	①
Suzuki 2016[8]	414	413	63.0	64.0	APD	AGD	高	①
Sun 2019[9]	50	50	未提及		APD	PD	高	①
Sugawara 2019[10]	195	195	67.0	66.0	FPD	PD	高	①
Tesaro 2016[11]	264	262	57.0±10.1	57.7±11.5	UGD	GD	高	①
Helsinn 2020[12]	200	202	55.6±9.9	55.2±9.7	FPD	NPD	高	①
张琳琳2016[13]	18	18	≤70		APD	ATD	高	①
谢王踢2018[14]	56	52	未提及		AGD	GD	高	①
Layman 2013[15]	20	20	>18		APD	AOD	高	①
孟文静2016[16]	78	78	54.0	51.0	ATD	TD	高	①
芦婷婷2018[17]	35	35	61.5±8.0		ATD	TD	高	①
Schwartzberg 2017[18]	126	126	61.8±9.4	61.1±10.6	FGD	FOD	中高	①
王涛2018[19]	40	40	48.5±1.1	48.6±1.2	ATD	TD	高	①
田欣2016[20]	25	25	53.0	51.0	ATD	TD	高	①
Schmitt 2014[21]	181	181	58.3	57.9	AGD	GD	高	①
Hu 2014[22]	211	210	53.1±10.1	53.6±10.6	AGD	GD	高	①
Campos 2001[23]	87	87	55.0±16.0	53.0±14.0	AGD	GD	高	①
赵宁莉2020[24]	316	316	57.0	55.0	FGD	AGD	高	①
齐婧2017[25]	35	37	36.0～67.0		ATD	TD	高	①
Herrington 2008[26]	22	21	59.6±10.7	58.3±10.5	APD	PD	高	①②
Kim 2017[27]	240	240	59.7±11.4	60.9±11.5	AOD	OD	中高	①②
Schmoll 2006[28]	242	242	59.0±11.0	58.0±11.0	AOD	OD	高	①②
Rapoport 2010[29]	415	415	57.1±11.8	55.9±12.6	AOD	OD	中高	①②
Poli-Bigelli 2003[30]	260	263	54.0±13.0	53.0±14.0	AOD	OD	高	①②
Maru 2013[31]	1 147	1 175	56.0	57.0	FOD	AOD	高	①②
Chang 2020[32]	339	328	54.4	54.9	NPD	AGD	高	①②
陈丽昆2015[33]	139	152	55.9±9.6	55.1±8.8	AGD	GD	高	①②
Yang 2017[34]	317	309	55.0	53.0	FGD	AGD	高	①②
Wenzell 2013[35]	20	20	18.0～89.0		APD	AOD	高	①②
Weinstein 2016[36]	500	500	60.0±11.8	59.1±12.3	FOD	OD	中高	①②
Hesketh 2016[37]	192	209	61.0	64.0	UGD	GD	高	①②③
Hesketh 2003[38]	260	260	59.0±12.0	58.0±12.0	AOD	OD	高	①②③
Herrstedt 2009[39]	479	479	52.0	51.0	KOD	OD	中高	①②③
Grunberg 2009[40]	270	271	59.0	59.0	KOD	OD	高	①②③
Ishido 2016[41]	42	42	65.0	64.0	AGD	PD	高	①②③
Warr 2005[42]	438	428	53.1±10.7	52.1±10.9	AOD	OD	中高	①②③
赵桂芳2017[43]	40	40	38.8±5.3	40.5±4.2	APD	PD	高	①②③
Zhang 2018[44]	412	416	54.6±9.6	54.5±10.2	NPD	AGD	高	①②③
Aapro 2014[45]	724	725	54.0	54.0	NPD	PD	高	①②③
Yeo2022[46]	60	62	56.0	46.5	NPD	AOD	高	①②③
Arpornwirat 2009[47]	120	121	57.0	58.5	KOD	OD	中高	①②③
Takahashi 2010[48]	146	150	60.5±9.7	63.3±9.4	AGD	GD	高	①②③
Schwartzberg 2015[49]	666	666	56.7±11.6	56.6±12.1	UGD	GD	中高	①②③
Saito 2013[50]	170	170	58.3	57.9	FGD	GD	高	①②③
Matsumoto 2020[51]	162	164	54.0	54.0	FPD	FGD	高	①②③
Zhang 2020[52]	324	324	55.9±10.4	55.8±10.2	FPD	APD	高	①②③
Kitayama 2015[53]	35	35	70.0	73.0	FGD	PD	中高	②③
Kaushal 2015[54]	30	30	52.0	51.0	APD	OD	高	②③
Hesketh 2012[55]	355	355	61.3±10.8	61.3±11.0	KOD	OD	高	②③
田奕2016[56]	21	21	55.2		APD	PD	中高	②③
潘国华2017[57]	60	62	62.3	63.6	AOD	OD	高	②③
曹峰2015[58]	30	30	40.0～71.0	42.0～73.0	FOD	OD	高	②③
丁洁2021[59]	31	31	40.0～75.0		FPD	PD	高	②③
张桂枫2015[60]	30	30	16.0～72.0		AGD	GD	高	②
陈铃2016[61]	39	39	42.5±7.1	43.1±6.9	APD	PD	高	②
Wang 2021[62]	125	118	57.1±8.6	56.2±8.4	APD	PD	高	②

①：急性CINV控制率；②：急性呕吐控制率；③：急性恶心控制率。

2.2　纳入文献质量评价结果

所有研究均为RCT[4－62]。42项研究描述了随机分配方法[5－6,8,10－12,15－16,18,21－42,44－45,47－53,55,62]；37项研究描述了分配隐藏[5－6,8,10－12,15,18,21－24,26－27,29－34,36－42,44－45,47－53,62]；35项研究描述了研究对象实施盲法和结果评估盲法[5－6,8,10－12,15,18,21－24,26－27,29－34,36－40,42,44－45,47－52,62]；51项研究结局数据完整[4－8,10－13,15－24,26－27,29－34,36－42,44－55,57－60,62]；所有研究均未选择性报告结果，均无明显发表偏倚（图略）。

2.3　网状Meta分析结果

2.3.1　各结局指标的证据关系图

59项研究均为双臂研究，结果见图2（以急性CINV控制率为例，图中直线表示进行直接比较的RCT，线段粗细表示直接比较的研究数，圆点表示干预措施，圆点大小表示实施该干预措施的样本量）。异质性检验结果显示，各研究结果无统计学异质性；一致性检验结果表明，各研究间一致性良好。

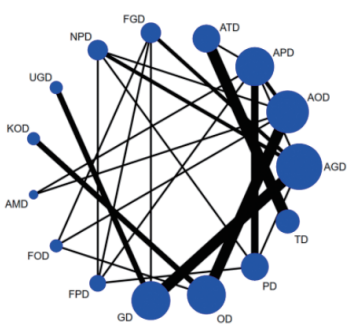

图2　急性CINV控制率的证据关系图

2.3.2　急性CINV控制率

49项研究报道了急性CINV控制率[4－52]，涉及15种干预措施。结果显示，使用三联方案患者的急性CINV控制率大多显著高于使用二联方案患者（$P<0.05$）；使用FPD患者的急性CINV控制率显著高于使用UGD、NPD、KOD、FOD、ATD、APD、AOD和AGD患者（$P<0.05$）；使用FGD患者的急性CINV控制率显著高于UGD、NPD、KOD、ATD、APD、AOD和AGD患者（$P<0.05$）。结果见图3。

2.3.3　急性呕吐控制率

37项研究报道了急性呕吐控制率[26－62]，涉及12种干预措施。结果显示，使用FPD患者的急性呕吐控制率显著高于使用NPD、KOD、FOD、AOD和AGD患者（$P<0.05$）。结果见图4。

2.3.4　急性恶心控制率

23项研究报道了急性恶心控制率[37－59]，涉及12种干预措施。结果显示，使用FPD患者的急性恶心控制率显著高于使用NPD、KOD、AOD和AGD患者（$P<0.05$）。结果见图4。

UGD													
9.32(1.74,49.84)[a]	TD												
1.50(0.95,2.39)	0.16(0.03,0.83)[a]	PD											
1.86(1.03,3.36)[a]	0.20(0.04,1.07)	1.24(0.75,2.04)	OD										
1.16(0.75,1.80)	0.12(0.02,0.64)[a]	0.77(0.60,0.99)[a]	0.62(0.38,1.01)	NPD									
1.26(0.65,2.46)	0.14(0.02,0.75)[a]	0.84(0.46,1.51)	0.68(0.50,0.92)[a]	1.09(0.61,1.93)	KOD								
1.40(1.08,1.81)[a]	0.15(0.03,0.79)[a]	0.93(0.63,1.37)	0.75(0.44,1.28)	1.21(0.84,1.72)	1.11(0.60,2.06)	GD							
0.53(0.33,0.86)[a]	0.06(0.01,0.29)[a]	0.35(0.26,0.48)[a]	0.29(0.17,0.48)[a]	0.46(0.33,0.63)[a]	0.42(0.23,0.77)[a]	0.38(0.25,0.57)[a]	FPD						
1.03(0.57,1.85)	0.11(0.02,0.59)[a]	0.69(0.42,1.13)	0.55(0.41,0.74)[a]	0.89(0.55,1.44)	0.82(0.53,1.25)	0.74(0.44,1.25)	1.94(1.17,3.24)[a]	FOD					
0.65(0.42,0.99)[a]	0.07(0.01,0.36)[a]	0.43(0.30,0.62)[a]	0.35(0.21,0.57)[a]	0.56(0.39,0.79)[a]	0.51(0.29,0.92)[a]	0.46(0.33,0.65)[a]	1.22(0.85,1.75)	0.63(0.39,1.01)	FGD				
4.73(0.93,24.00)	0.51(0.34,0.77)[a]	3.15(0.64,15.39)	2.54(0.50,12.96)	4.08(0.83,19.99)	3.75(0.72,19.69)	3.38(0.68,16.82)	8.92(1.81,43.88)[a]	4.59(0.90,23.41)	7.30(1.47,36.17)[a]	ATD			
0.95(0.60,1.49)	0.10(0.02,0.51)[a]	0.63(0.47,0.85)[a]	0.51(0.32,0.82)[a]	0.82(0.60,1.12)	0.75(0.43,1.32)	0.68(0.46,0.99)[a]	1.79(1.29,2.48)[a]	0.92(0.57,1.47)	1.46(1.02,2.10)[a]	0.20(0.04,0.95)[a]	APD		
1.06(0.60,1.88)	0.11(0.02,0.61)[a]	0.71(0.44,1.13)	0.57(0.47,0.69)[a]	0.92(0.58,1.44)	0.84(0.59,1.21)	0.76(0.46,1.27)	2.00(1.23,3.27)[a]	1.03(0.79,1.35)	1.64(1.03,2.61)[a]	0.22(0.04,1.13)	1.12(0.72,1.74)	AOD	
0.84(0.45,1.56)	0.09(0.02,0.48)[a]	0.56(0.33,0.94)[a]	0.45(0.28,0.73)[a]	0.72(0.43,1.22)	0.67(0.38,1.18)	0.60(0.34,1.06)	1.58(0.92,2.71)	0.81(0.49,1.34)	1.29(0.76,2.22)	0.18(0.03,0.90)[a]	0.89(0.56,1.41)	0.79(0.50,1.23)	AMD
0.86(0.60,1.24)	0.09(0.02,0.48)[a]	0.58(0.43,0.78)[a]	0.47(0.29,0.75)[a]	0.75(0.58,0.97)[a]	0.69(0.39,1.22)	0.62(0.48,0.80)[a]	1.63(1.17,2.27)[a]	0.84(0.52,1.35)	1.33(1.01,1.77)[a]	0.18(0.04,0.89)[a]	0.91(0.68,1.22)	0.81(0.52,1.28)	1.03(0.62,1.72)

AGD

a：$P<0.05$。

图3　急性CINV控制率的网状Meta分析结果

UGD	1.18(0.68,2.04)	1.94(0.86,4.35)	1.17(0.70,1.96)	1.48(0.64,3.39)	1.01(0.82,1.24)	0.60(0.33,1.07)	1.08(0.19,6.08)	0.83(0.52,1.30)	0.69(0.36,1.31)	1.60(0.72,3.55)	1.17(0.73,1.87)
2.16(1.18,3.93)[a]	PD	1.64(0.82,3.31)	0.99(0.74,1.32)	1.25(0.60,2.59)	0.85(0.51,1.42)	0.51(0.29,0.87)[a]	0.91(0.17,4.91)	0.70(0.41,1.18)	0.58(0.34,1.00)	1.36(0.69,2.69)	0.99(0.68,1.44)
2.51(1.06,5.97)[a]	1.17(0.57,2.39)	OD	0.60(0.31,1.17)	0.76(0.63,0.93)[a]	0.52(0.24,1.14)	0.31(0.14,0.67)[a]	0.56(0.12,2.57)	0.43(0.19,0.94)[a]	0.36(0.17,0.74)[a]	0.83(0.65,1.05)	0.60(0.30,1.23)
1.37(0.79,2.37)	0.64(0.47,0.86)[a]	0.55(0.28,1.08)	NPD	1.27(0.63,2.54)	0.86(0.54,1.39)	0.51(0.29,0.89)[a]	0.92(0.17,4.91)	0.71(0.42,1.19)	0.59(0.34,1.04)	1.38(0.72,2.63)	1.00(0.76,1.32)
1.37(0.54,3.44)	0.63(0.29,1.39)	0.54(0.40,0.75)[a]	1.00(0.47,2.12)	KOD	0.68(0.30,1.53)	0.40(0.18,0.90)[a]	0.73(0.16,3.41)	0.56(0.25,1.26)	0.47(0.22,0.99)[a]	1.09(0.80,1.48)	0.79(0.38,1.65)
1.55(1.19,2.04)[a]	0.72(0.42,1.23)	0.62(0.27,1.41)	1.13(0.70,1.82)	1.14(0.47,2.74)	GD	0.59(0.34,1.02)	1.07(0.19,5.97)	0.82(0.54,1.23)	0.69(0.37,1.26)	1.59(0.74,3.43)	1.16(0.76,1.78)
0.48(0.23,1.01)	0.22(0.13,0.38)[a]	0.19(0.08,0.43)[a]	0.35(0.20,0.63)[a]	0.35(0.15,0.85)[a]	0.31(0.15,0.62)[a]	FPD	1.80(0.32,10.03)	1.38(0.89,2.15)	1.16(0.74,1.80)	2.69(1.25,5.78)[a]	1.95(1.11,3.44)[a]
1.21(0.50,2.93)	0.56(0.27,1.17)	0.48(0.37,0.63)[a]	0.88(0.43,1.79)	0.88(0.58,1.34)	0.78(0.33,1.81)	2.51(1.08,5.83)[a]	FOD	0.77(0.14,4.29)	0.64(0.12,3.49)	1.49(0.32,7.01)	1.08(0.20,5.86)
0.57(0.32,1.01)	0.26(0.15,0.46)[a]	0.23(0.10,0.53)[a]	0.42(0.25,0.70)[a]	0.42(0.17,1.02)	0.37(0.22,0.61)[a]	1.19(0.62,2.29)	0.47(0.20,1.12)	FGD	0.84(0.48,1.47)	1.94(0.89,4.23)	1.41(0.85,2.36)
0.71(0.35,1.46)	0.33(0.21,0.53)[a]	0.28(0.13,0.60)[a]	0.52(0.31,0.88)[a]	0.52(0.23,1.17)	0.46(0.23,0.89)[a]	1.48(0.93,2.34)	0.59(0.27,1.27)	1.24(0.64,2.41)	APD	2.32(1.12,4.81)	1.69(0.94,3.04)
1.19(0.51,2.80)	0.55(0.27,1.12)	0.47(0.40,0.57)[a]	0.87(0.44,1.70)	0.87(0.60,1.25)	0.77(0.34,1.73)	2.48(1.10,5.58)[a]	0.99(0.78,1.25)	2.09(0.91,4.79)	1.68(0.80,3.52)	AOD	0.73(0.36,1.46)
1.06(0.66,1.71)	0.49(0.34,0.72)[a]	0.42(0.20,0.88)[a]	0.77(0.58,1.02)	0.78(0.35,1.72)	0.68(0.46,1.01)	2.21(1.21,4.05)[a]	0.88(0.41,1.87)	1.86(1.16,2.98)[a]	1.50(0.85,2.63)	0.89(0.43,1.83)	AGD

a：$P<0.05$；灰色：急性呕吐控制率；绿色：急性恶心控制率。

图4　急性呕吐控制率和急性恶心控制率的网状Meta分析结果

2.3.5　不同干预措施的网状Meta分析排序结果

急性CINV控制率的SUCRA由高到低排序依次为FPD（98.6%）、FGD（91.6%）、AMD（75.3%）、AGD（74.7%）、APD（65.9%）、UGD（60.3%）、FOD（58.3%）、AOD（55.1%）、KOD（49.6%）、NPD（46.8%）、GD（30.7%）、PD（25.6%）、OD（16.0%）、ATD（11.0%）、TD（0.7%）；急性呕吐控制率排序依次为FPD（96.1%）、FGD（89.9%）、APD（80.1%）、UGD（61.3%）、AGD（58.4%）、AOD（50.2%）、FOD（48.1%）、KOD（37.2%）、NPD（36.8%）、GD（27.7%）、PD（9.4%）、OD（4.8%）；急性恶心控制率排序依次为FPD（93.6%）、APD（84.6%）、FGD（74.2%）、UGD（56.8%）、GD（56.0%）、FOD（51.6%）、NPD（42.6%）、AGD（41.7%）、PD（41.0%）、KOD（30.0%）、AOD（21.9%）、OD（5.9%）。结果表明，在帕洛诺司琼/格拉司琼+地塞米松的基础上联合福沙匹坦的效果更佳。

2.4　发表偏倚分析

对各指标绘制倒漏斗图。结果显示，各研究散点均在倒漏斗图范围内，基本对称，提示本研究存在发表偏倚的可能性较小（图略）。

3　讨论

国家癌症中心公布的报告显示，2015年我国新发恶性肿瘤约392.9万例，死亡约233.8万例[1]。目前，化疗仍是各种恶性肿瘤的主要治疗手段，而化疗引起的CINV是最常见的不良反应之一。由于化疗周期较长，长期反复发生CINV会降低患者的依从性和生存质量，从而影响治疗效果和预后。在我国，CINV的防治以5-HT_3受体拮抗剂联合地塞米松为主，但仍有30%患者的CINV未得到有效控制[1]。《中国肿瘤药物治疗相关恶心呕吐防治专家共识（2022年版）》[1]建议首选三联方案防治由高度致吐风险化疗药物所致的急性CINV。

本研究结果显示，在急性CINV控制率方面，以FPD最优，其次为FGD和AMD。在急性呕吐控制率方面，以FPD最优，其次为FGD和APD。在急性恶心控制率方面，以FPD最优，其次为APD和FGD。这提示，中高度致吐风险化疗药物所致的CINV中，FPD为最优治疗方案。循证证据表明，帕洛诺司琼用于预防急性CINV的疗效优于第一代5-HT_3受体拮抗剂，这可能与其具有更强的亲和力及更长的半衰期（40 h）密切相关[63]。福沙匹

坦和阿瑞匹坦均为NK-1受体拮抗剂，福沙匹坦是口服制剂阿瑞匹坦的前体药物，注射后在体内经代谢迅速转化为阿瑞匹坦，二者疗效相似。

既往虽有Meta分析对不同化疗止吐方案进行评价，但存在纳入干预措施单一，研究数量较少，导致临床指导价值较低等不足。与既往Meta分析相比，本研究检索更充分，纳入的干预措施更全面。但本研究也存在不足之处：(1)不同三联方案头对头比较的研究数量较少，多通过间接比较进行效应量合并；(2)不同研究对结局事件的判断标准可能存在差异，无法对每个研究进行基于个体化水平的分析，导致结果可能存在一定偏倚。

综上所述，FPD较其他三联方案和二联方案防治中高度致吐风险化疗药物所致的急性CINV疗效最好。

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