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Evaluatingthe Outcome of Total Intravenous Anesthesia and Single Drug Pharmacological to Prevent Postoperative Vomiting: Systematic Review and Meta-Analysis

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Abstract

Background and aim: the aim of present systematic review and meta-analysis was evaluate the outcome of total intravenous anesthesia and single-drug pharmacological to prevent postoperative vomiting in children and adult.

Method: From the electronic databases, PubMed, Cochrane Library, Embase have been used to perform a systematic literature until May 2021. For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. Moreover risk ratio with 95% confidence interval (CI), fixed effect model and Mantel-Haenszel method were calculated. The Meta analysis have been evaluated with the statistical software Stata/MP v.16 (The fastest version of Stata).

Result:A total of 224 potentially relevant titles and abstracts were found during the electronic search. Finally, nine studies required for this systematic review. Risk ratio of postoperative nausea and vomiting in adult and children was 0.03 (RR, 0.03 95% CI -0.22, 0.27. P= 0.81) and -0.07 (RR, -0.07 95% CI -0.30, 0.17. P= 0.59), respectively.

Conclusion: Present systematic review and meta-analysis showed there was no statistically significant difference between total intravenous anesthesia and single-drug pharmacological to prevent postoperative nausea and vomiting in children or in adults. Finally, it can be concluded that total intravenous anesthesia had equally effective compared with Single pharmacological prophylaxis to reduce PONV in children and adults.

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Keywords:total intravenous anesthesia, Postoperative nausea and vomiting, single-drug pharmacological

Introduction

Postoperative nausea and vomiting (PONV) is one of the most common complications after general anesthesia in children and adults(1). PONV is a patient-important outcome; patients often rate PONV as worse than postoperative pain. PONV usually resolves or is treated without sequelae, but may require unanticipated hospital admission and delay recovery room discharge(2). Statistics show that about 30% of children over 3 years of age experience PONV, in certain surgeries such as strabismus surgery, the incidence of PONV is about 70% and higher(3). Studies show that PONV is not usually diagnosed in children because children do not consider nausea to be a cause of discomfort(4).PONV can be the only diagnostic symptom in children that can increase the length of hospital stay(5).Studies show that PONV can increase hospitalization time and increase post-anesthesia care. There are guidelines for preventing and reducing PONV(6). Prevention is one of the important factors in reducing patients' discomfort, also prophylaxis is based on a poly-pragmatic approach. Studies show that anesthesiologists tend to avoid inhaled anesthetics and propofol-based total intravenous anesthesia(7).Placement of an intravenous access is a difficult strategy and challenging in children. (8, 9). In this case, face mask induction with inhaled anesthetics is used. Given the importance of the issue and its challenge, the aim of present systematic review and meta-analysis was evaluate the outcome of total intravenous anesthesia and single-drug pharmacological to prevent postoperative vomiting in children and adult.

Methods

Search strategy

From the electronic databases, PubMed, Cochrane Library, Embase, have been used to perform a systematic literature until May 2021. Therefore, a software program (Endnote X8) has been utilized for managing the electronic titles. Searches were performed with mesh terms:

("Anesthesia, Intravenous"[Mesh]) AND ("Postoperative Nausea and Vomiting/complications"[Mesh] OR "Postoperative Nausea and Vomiting/drug therapy"[Mesh] OR "Postoperative Nausea and Vomiting/surgery"[Mesh] OR "Postoperative Nausea and

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Vomiting/therapy"[Mesh])) AND ("Child"[Mesh] OR "Adult Children"[Mesh] OR "Child, Hospitalized"[Mesh])) OR ("Adult"[Mesh] OR "Young Adult"[Mesh])) AND "Anesthesia, General"[Mesh]) AND "Pharmacology"[Mesh]) OR ("Post-Exposure Prophylaxis"[Mesh] OR "Pre-Exposure Prophylaxis"[Mesh]) .

In other databases, the search was performed with the keyword Anesthesia, general anesthesia, total intravenous anesthesia, single pharmacological prophylaxis, postoperative vomiting, postoperative nausea, postoperative nausea and vomiting, PONV, children, adult and pediatric patients.

This systematic review has been conducted on the basis of the key consideration of the PRISMA Statement–Preferred Reporting Items for the Systematic Review and Meta-analysis(10), and PICO strategy (Table1).

Selection criteria

Inclusion criteria

1. Randomized controlled trials studies, controlled clinical trials, prospective and retrospective cohort studies.
2. Postoperative nausea and vomiting
3. Inhalational anesthesia with single-drug pharmacological prophylaxis
4. propofol-based total intravenous anesthesia
5. English language

Exclusion criteria

1. In vitro studies, reviews, animal studies and clinical studies
2. Incomplete or inconsistent data for the purpose of the present study.

Table1. PICO strategy

PECO strategy	**Description**
P	Population: patients who underwent surgery
I	Intervention: total intravenous anesthesia
C	Comparison: inhalational anesthesia
O	Outcome:Postoperative nausea and vomiting

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Data Extraction and method of analysis

The data have been extracted from the research included with regard to the study, years, study design, sample size,type of surgery, maintenance, examination group, and control group.

Cochrane Collaboration's tool (11) used to assessed quality of the RCT studies that included in Present meta-analysis. The scale scores for low risk was 1 and for High and unclear risk was 0, Scale scores range from 0 to 6 and higher score means higher quality. Methodological Index for Non-Randomized Studies (MINORS) used to assess quality of the Non-RCT studies, higher score than 16 means higher quality of study.

For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. Prior to the screening, kappa statistics was carried out in order to verify the agreement level between the reviewers. The kappa values were higher than 0.80.

Moreover mean difference and risk ratio with 95% confidence interval (CI), fixed or random effect model and Inverse-variance or Mantel-Haenszel or REML method were calculated. Random effects were used to deal with potential heterogeneity and I^2 showed heterogeneity. I^2 values above 50% signified moderate-to-high heterogeneity. The Meta analysis have been evaluated with the statistical software Stata/MP v.16 (The fastest version of Stata).

Results

According to the purpose of the study, in the initial search with keywords, 224 articles were found. In the first step of selecting studies, 223 studies were selected to review the abstracts. Then, studies that did not meet the inclusion criteria were excluded from the study. In the second step, the full text of 39 studies was reviewed. Finally, nine studies were selected (Figure1).

Characteristics

Nine studies (randomized controlled trial) have been included in present article, five studies evaluated outcome of TINA and IA+AE to prevent PONV in adult and four studies evaluated outcome of TINA and IA+AE to prevent PONV in children. The Number of adult patients in TINA group was 284 and in IA+AE group was 296, a total was 580 with mean of 39.5 years. In four studies the type of surgery was Gynaecologic laparoscopy and in one study was laparotomic abdominal surgery. The Number of children patients in TINA group was 314 and in IA+AE

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group was 244, a total was 558 with mean of 7.1 years. In all studies the type of surgery was Strabismus surgery (Table2).

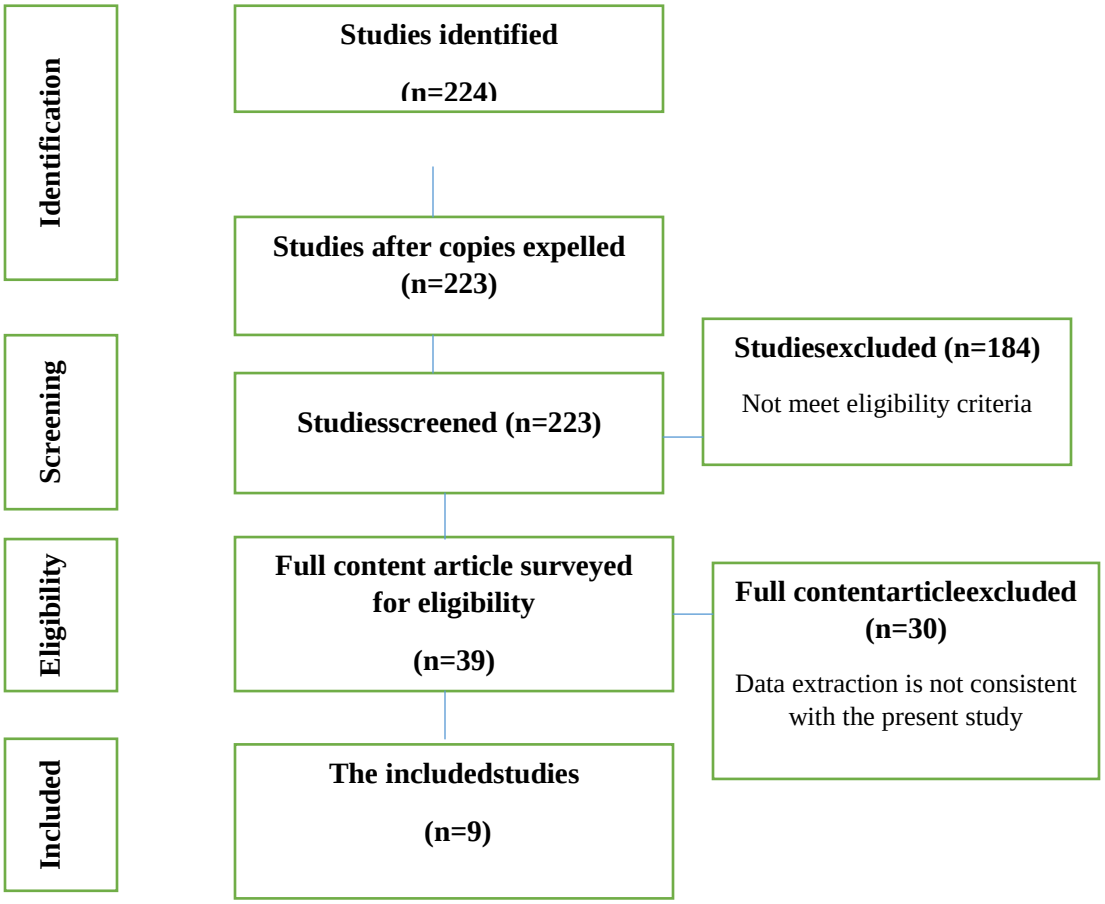

Figure 1. Study Attrition

Bias assessment

According to Cochrane Collaboration's tool, six studies had a total score of 3/6 (moderate risk of bias) and two studies had a total score of 2/6 (high risk of bias). This result showed moderate to low quality in studies that included in present article (Table3).

Table2. Studies selected for systematic review and meta-analysis

Study. Years	Study design	Number of patients		Mean/rang of age (years)	method	Type of surgry
		TIVA	IA +			

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			AE			
Amiri et al.,2020 (12)	RCT	52	53	18 – 65 46.4	Midazolam 0.02 mg.kg-1 fentanyl 2 g.kg-1 intravenous thiopental sodium 5 mg.kg-1, atracurium 0.5 mg.kg-1 Isoflurane 1.5%−1.7% in	laparotomic abdominal surgery
Mei et al., 2014(13)	RCT	74	74	57 to 99 58	Propofol with remifentanil, titrated Sevoflurane with remifentanil titrated	Gynaecologic laparoscopy
Park et al., 2011 (14)	RCT	50	50	18-80 37	Propofol with remifentanil Sevoflurane with 50% N2O	Gynaecologic laparoscopy
White et al., 2007(15)	RCT	58	68	26 to 59 39	Propofol with fentanyl Sevoflurane with fentanyl	gynaecologic surgery
Purhonen et al., 2006 (16)	RCT	50	51	30-7- 59	Propofol with fentanyl Isoflurane with fentanyl and 67% N2O	Gynaecologic laparoscopy
Klockgether-Radke et al., 1995(17)	RCT	60	30	9.8	Propofol with alfentanil, additional 67% N2O Halothane with 67% N2O	Strabismus surgery
Splinter et al., 1997 (18)	RCT	156	144	6.0	Propofol with 70% N2O	Strabismus surgery
Tramer et al., 1998 (19)	RCT	38	40	7.3	Propofol with alfentanil	Strabismus surgery
Watcha et al., 1991 (20)	RCT	60	30	4.6	Propofol, additional 66% N2O	Strabismus surgery

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Overall postoperative nausea and vomiting

Adults:

Risk ratio of postoperative nausea and vomiting in adult was 0.03 (RR, 0.03 95% CI -0.22, 0.27. P= 0.81) among four studies and heterogeneity found (I^2=76.86%; P =0.00). This result showed there was no statistically significant difference between TIVA and control group (Figure2).

Children:

Risk ratio of postoperative nausea and vomiting in children was -0.07 (RR, -0.07 95% CI -0.30, 0.17. P= 0.59) among four studies and heterogeneity found (I^2=54.01%; P =0.09). This result showed there was no statistically significant difference between TIVA and control group (Figure3).

Table3. Risk of bias assessment (Low (+), unclear (?), high (-))

study	Random sequence generation	allocation concealme	blinding of participant s and	blinding of outcome assessment	incomplete outcome	selective reporting	Total score
Amiri et al.,2020 (12)	+	?	+	?	+	+	3
Mei et al., 2014 (13)	+	?	?	+	?	+	3
Park et al., 2011 (14)	+	?	?	+	?	+	3
White et al., 2007 (15)	+	+	+	-	?	?	3
Purhonen et al., 2006 (16)	?	+	+	?	?	+	3
Klockgether-Radke et al., 1995(17)	?	?	?	+	?	+	2
Splinter et al., 1997 (18)	+	?	?	?	+	-	2
Tramer et al., 1998 (19)	?	+	?	+	+	?	3

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Watcha et al., 1991 (20)	?	?	?	+	+	?	2

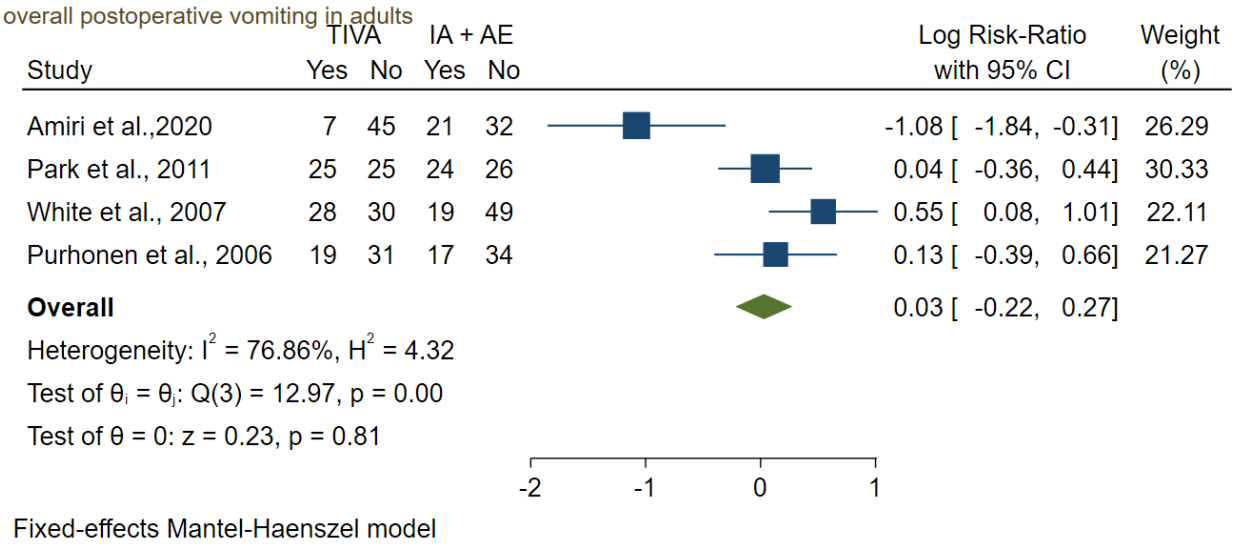

Figure2. Forest plot showed overall postoperative nausea and vomiting in adults

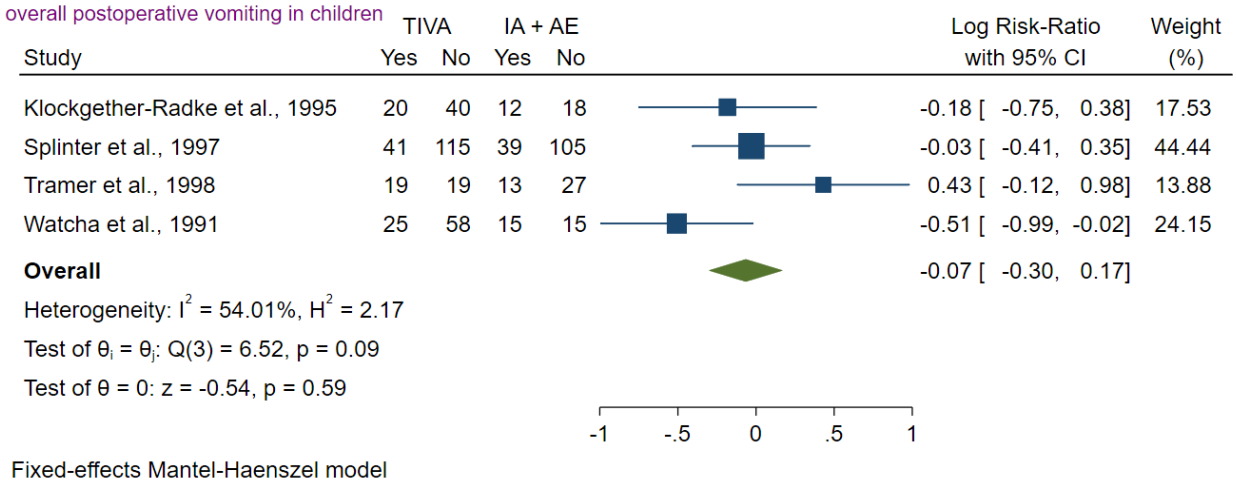

Figure3. Forest plot showed overall postoperative nausea and vomiting in children

Postoperative adverse events

Adults:

Subgroup meta-analysis:

Risk ratio of vomiting in adult was 0.14 (RR, 0.14 95% CI -0.37, 0.64) among three studies and heterogeneity found (I^2=40.96%; P =0.18). Risk ratio of need for rescue medication in adult was

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0.14 (RR, 0.14 95% CI -0.31, 0.59) among three studies and heterogeneity found (I^2<0%; P =0.45). Risk ratio of early PONV in adult was 0.09 (RR, 0.09 95% CI -0.23, 0.41) among four studies and heterogeneity found (I^2=0%; P =0.72). Risk ratio of late PONV in adult was 0.35 (RR, 0.35 95% CI -0.02, 0.73) among four studies and heterogeneity found (I2=55.58%; P =0.08). Overall risk ratio of postoperative adverse events in adults was 0.18 (RR, 0.18 95% CI -0.02, 0.38); heterogeneity found (I^2=7.01%; P =0.38) and there was no statistically significant difference between groups (p=0.75)(Figure4).

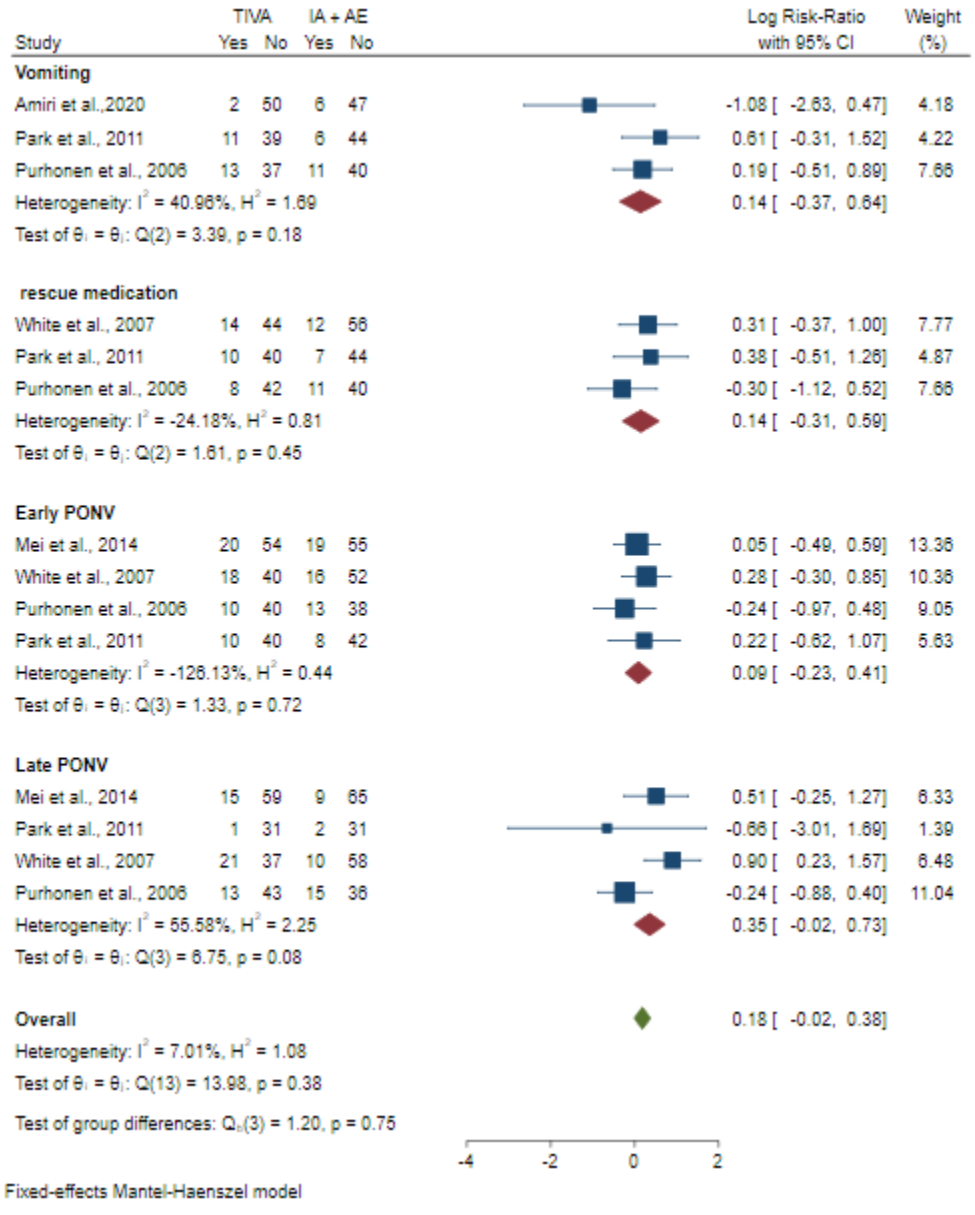

Figure4. Forest plot showed Postoperative adverse events in adults

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Children:

Subgroup meta-analysis:

Risk ratio of early PONV in Children was 0.44 (RR, 0.44 95% CI -0.09, 0.97) among four studies and heterogeneity found (I^2=27.54%; P =0.25). Risk ratio of late PONV in children was -0.11 (RR, -0.11 95% CI -0.58, 0.35) among two studies and heterogeneity found (I^2<0%; P =0.87). Overall risk ratio of postoperative adverse events in children was 0.16 (RR, 0.16 95% CI -0.19, 0.51); heterogeneity found (I^2=19.26%; P =0.29) and there was no statistically significant difference between groups (p=0.13) (Figure5).

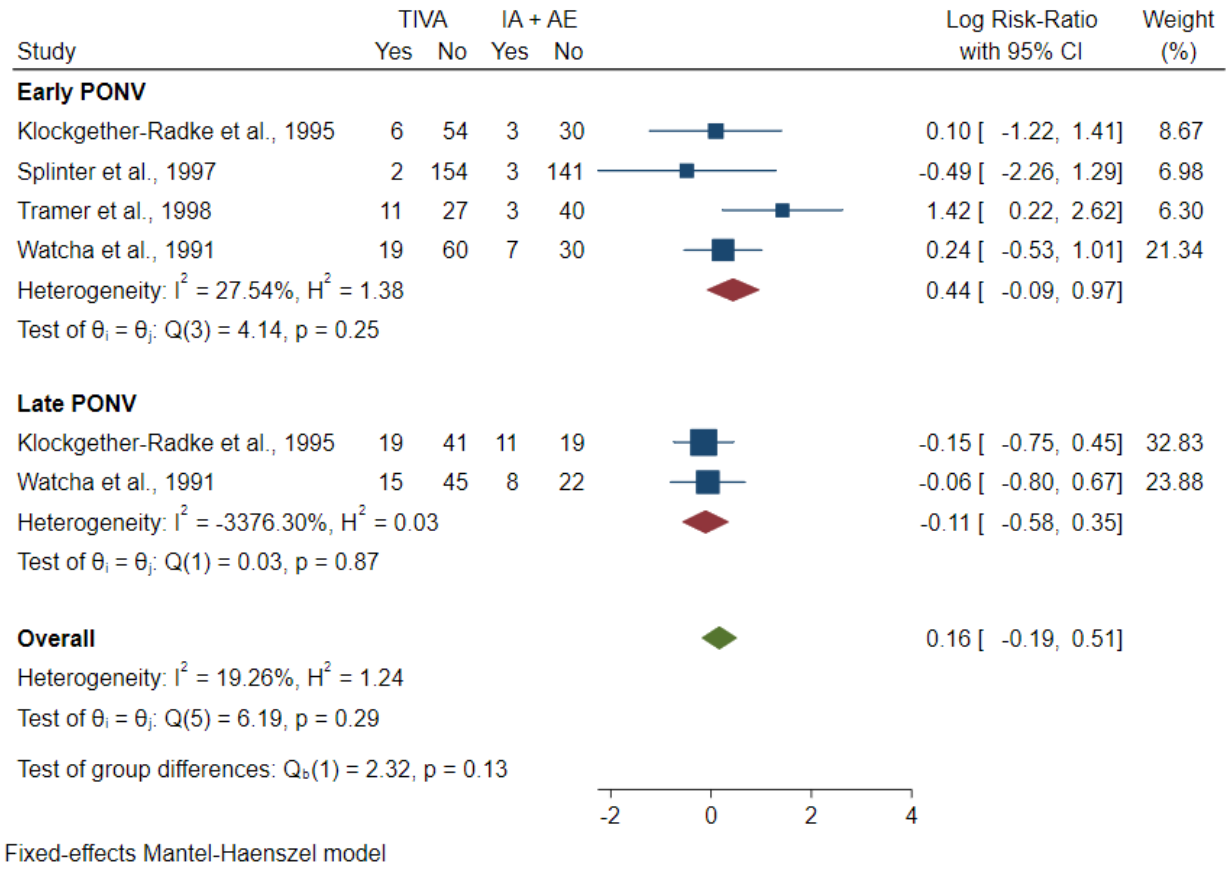

Figure5. Forest plot showed Postoperative adverse events in children

Discussion

The aim pf present systematic review and meta-analysis was evaluate the outcome of total intravenous anesthesia and single-drug pharmacological to prevent postoperative vomiting in children and adult. The Meta analysis showed, there was no difference in the risk of PONV

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between the groups that received TIVA or IA +AE in adults or children. There was no difference between the groups that received TIVA or IA +AE in adults to need for rescue medication, early PONV. Patients receiving TIVA had a significantly higher risk of experiencing PONV in the late postoperative phase. There was no difference in the risk of PONV between the groups that received TIVA or IA +AE in children and not differ between groups in early and late PONV. Schaefer et al., 2016(21) and 2017(22) showed no difference in the overall risk of PONV in adult and children, these results are similar to the present study. PONV, are clinically relevant side effects after general anesthesia. This is true not only for adult patients, but especially for children as the incidence is even twice as high as for adults(1). Very old and few studies were found in the study of two groups of children who did not have high quality studies, so it is recommended that more studies be done in this area to provide strong data to examine prevention strategies to prevent PONV. Available in pediatric patients. Also, high quality studies and more similar methods are needed in the adult population to provide sufficient and strong evidence. It should be noted that this study did not seek to find the most effective PONV prevention strategy, but to compare which of the two groups was more effective than the other. Studies have reported other strategies in reducing PONV, especially in children, such as high doses of intravenous fluids, addition of regional anesthetic blocks (23-26).At present, specialists rarely use primary antiemetic prophylaxis in children for fear of side effects. Studies have shown that the effect of almost all pharmacological antiemetic prophylaxis is clinically equal, especially droperidol, ondansetron and dexamethasone (6, 27). Although PONV in adults and children is probably based on similar pathophysiology, we cannot assume that prophylaxis prescribed in adults is equally effective in children (22, 28-30). A study showed that the use of dexamethasone and ondansetron, the drug perididol, are ineffective in preventing nausea and vomiting(31). Unlike droperidol, other antiemetic drugs commonly used in adult patients have been shown to be effective in pediatric patients: Dexamethasone reduces the risk of PONV by up to 50% in children after tonsillectomy compared with placebo(32). In addition, the 5-HT 3 antagonists ondansetron, granisetron, tropisetron and dolasetron have been shown to be effective in preventing POV in children(33, 34). The present study had limitations such as low and medium quality studies, high risk of bias in two studies and modaret risk of bias in the rest of the selected studies, very few and old studies were found in the pediatric population. It is suggested that more RCT studies be performed in the adult and pediatric population, that the sample size be

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increased, that the procedure be similar, and that the quality of studies in this field be increased so that strong and sufficient evidence can be provided.

Conclusion

Present systematic review and meta-analysis showed there was no statistically significant difference between total intravenous anesthesia and single-drug pharmacological to prevent postoperative nausea and vomiting in children or in adults. Neither strategy alone can significantly reduce PONV in children or adults; the use of multiple prevention methods should be considered to reduce the incidence of PONV and improve the outcome of surgery. Finally it can be concluded that total intravenous anesthesia had equally effective compared with Single pharmacological prophylaxis to reduce PONV in children and adults.

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