Desflurane versus sevoflurane in pediatric anesthesia

ASSIGN BUSTER

Abstract

Objectives : Meta analysis to compare the effect of desflurane versus sevoflurane in pediatric anesthesia.

Methods: Rev. Man 5. 1 and Stata 11. 0 software were applied for the meta-analysis. Weighted mean difference (*WMD*) or odds ratio (*OR*) and 95% confidence intervals (*CI*) of for relevant indexes of patients with fractures of radial head were collected andcalculated in afixed-effects model (the Mantel-Haenszel method) or a random-effects model (the DerSimonian and Laird method) when appropriate.

Results: A total of 12 studies (14 comparisons) including 1311 children in pediatric anesthesia (experimental group: 649; control group: 662) were performed in the meta-analysis. The overall meta-analysis showed that there were significant differences of postoperative extubation time (*WMD* =-3. 87, 95% *CI* =-6. 14 to -1. 60, *P* <0. 01), eye opening time (*WMD* =-1. 11, 95% *CI* =-1. 49 to -0. 72, *P* <0. 01), awakening time (*WMD* =-4. 27, 95% *CI* =-5. 28 to -3. 26, *P* <0. 01) and agitation (*RR* = 1. 44, 95% *CI* = 1. 05 to 1. 96, *P* <0. 05) in children between the two groups, the results also suggested that there were no significant differences of discharge from the reciveryroom (*WMD* =-1. 92, 95% *CI* =-5. 83 to 1. 99, *P* > 0. 05), oculocardiac reflex (*RR* = 1. 03, 95% *CI* = 0. 75 to 1. 40, *P* > 0. 05), nausea and vomiting (*RR* = 1. 12, 95% *CI* = 0. 78 to 1. 62, *P* > 0. 05), severe pain (*RR* = 0. 95, 95% *CI* = 0. 68 to 1. 33, *P* > 0. 05) in children between the two groups.

Conclusions: Our results suggested that postoperative extubation time, eye opening time and awakening time of pediatric anesthesia in experimental

group may be lower than control group, agitation of pediatric anesthesia in experimental group may be higher than control group.

Key words: Desflurane; Sevoflurane; Meta-analysis

Introduction

General anesthesia allows dental treatment to be rendered under optimal conditions, theoretically ensuring ideal outcomes [1]. Spinal anesthesia in pediatrics began to be used in the late nineteenth century in multiple procedures, with priority for high-risk and former preterm infants, for its suggested protective role compared to the development of postoperative apnea with general anesthesia [2]. Although systemic analgesic therapies are the mainstay of pain treatment in pediatric palliative care, there are cases where they fail to adequately relieve symptoms or produce side effects that undermine effectiveness [3]. The use of regional anesthesia is increasingly common in pediatric practice [4]. Complications in pediatric anesthesia can happen, even in our modern hospitals with the most advanced equipment and skilled anesthesiologists [5]. Desflurane has the most rapid onset and offset of action among the volatile anesthetic agents used for general anesthesia, but it can cause airway reactivity, tachycardia, and hypertension during induction, especially in pediatric patients [6].

Whether the effect of desflurane in pediatric anesthesia is superior to sevoflurane is controversial [7-10]. In order to achieve an integrative understanding of effect difference between desflurane and sevoflurane with patients, it is necessary to consider the findings as a whole, giving attention to methodological characteristics of the studies. Accordingly, we conducted a

systematic review on published findings and used meta-analysis techniques to combine the results.

Methods

Data sources

We retrieved the relevant trials up to July 2014 from several public databases, mainly including PubMed, Medline, Springer, Elsevier Science Direct, Cochrane Library and Google scholar. The key words of “ desflurane”, “ sevoflurane”, “ pediatric anesthesia”, “ children”, “ study” and “ trial” were used for searching. Meanwhile, references from retrieved papers were checked for additional studies. We collected data from the full-published English papers, not any meeting or conference abstract.

Six investigators independently retrieved the electronic databases. An independent PubMed and Medline retrieve was done by A and B with the same method. An independent Springer and Elsevier Science Direct retrieve was done by C and D with the same method. An independent Cochrane Library and Google scholar retrieve was done by E and F with the same method. The abstracts were retrieved independently by two investigators (A and D) to determine whether they met the eligibility criteria for inclusion. References in the studies were reviewed by C and F to identify additional studies.

Assume that differences occur (Such as the included literature was not consistent with another investigator), a third investigator (E) will make additional assessment. If the third investigator’ assessment was consistent

with one of them, then the discussion should be made for the final decision of the included literatures.

Inclusion and exclusion standards of studies

Investigations with children in pediatric anesthesia (randomized controlled trial), the comparison between experimental group (desflurane) and control group (sevoflurane) were provided in papers, the effect size of postoperative extubation time, eye opening time, awakening time, discharge from the reciveryroom were weighted mean difference (*WMD*), the effect size of the number of oculocardiac reflex (OCR), agitation, nausea and vomiting, severe pain were odds ratio (*OR*), sample size or range of age were not limited. We excluded the studies in which just only described sevoflurane data or desflurane data with review or report, reduplicated studies or records, and the studies in which did not compared experimental group vs. control group.

Evaluation of quality and Extraction of data

Evaluation of quality mainly included the methods of studies, sample size, recruitment of studies. Firstly, we selected by reading the document title and abstract. In addition, we read the full text of papers for secondary screening, and then determined whether the studies were conformed to the inclusion standards. Two investigators independently completed the above issues. Assume that differences occur (Such as the extracted data or information was not consistent with another investigator), an agreement were reached by discussion.

We developed and extracted thedataafter we made training to all investigators. Data items included study details (e. g., the First author's name, research year of study, year of study publication, location of participants, design of studies.), and characteristics of participants (e. g., age, gender and sample size). Two investigators (A and D) extracted the data independently using the standard protocol, and the third investigator (E) reviewed their results of studies. We contacted authors of incorporated studies to obtain further information for data items that needed clarification. Discrepancies were resolved by discussing within our research team or contracting with the original investigators via e-mail. We recorded the first author's name, year of publication, sample size, intervention measure and mean age of patients in experimental group vs. control group.

Meta-analysis methods

The meta-analysis was performed in fixed or random effect models. Risk Ratio (*RR*) or weighted mean difference (*WMD*) and its 95% confidence interval (95% *CI*) were estimated with each study. The overall or pooled estimate of *ORs* or *WMDs* was obtained using Mantel–Haenszel method in the fixed effect model [11] or using DerSimonian and Laid method in the random effect model [12]. We assessed the within- and between-study variation or heterogeneity by testing Cochran's Q-statistic [13]. We also quantified the effect of heterogeneity using $I^2 = 100\ \% \times (Q - \mathrm{df})/Q$ [14]. A significant Q-statistic ($P < 0.10$) or I^2-statistic ($I^2 > 50\%$) indicated heterogeneity across the studies, and then the random effects model was used for meta-analysis. Otherwise, the fixed effects model was used.

The meta-analysis was performed using the software of Review Manager 5. 1 (Cochrane Collaboration, http://ims. cochrane. org/revman), and the publication bias of the included studies were calculated using the STATA package v. 11. 0 (Stata Corporation, College Station, TX, USA). All the *P* – values were two-sided. The *P* value less than 0. 05 was considered to be significant statistically, while the *P* value less than 0. 1 was considered to be significant statistically in heterogeneity analysis.

Evaluation of publication bias

We evaluated the publication bias using Egger's linear regression test [15], which measures funnel plot asymmetry by the natural logarithm scale of the effect size.

Results

C haracteristics of eligible studies

There were 871 papers potentially relevant to the search terms (PubMed: 265; Medline: 126; Springer: 151; Elsevier Science Direct: 107; Cochrane Library: 12; Google Scholar: 210.) The study selection process is shown in Figure 1. There were 85 potentially relevant studies after removing duplicatesor irrelevant studies. During the step of screening the abstracts, 54 of these articles were excluded (23 were review articles; 21 not RCT). Then 31 studies were left for full publication review, 19 of which were excluded (12 only reported desflurane data but not for comparison; 7 provided no available data).

As is shown in Table 1, there were12 studies [7-10, 16-23] (14 comparisons) in the meta-analysis, and the characteristics of included studies were presented. The included studies were published between 1996 and 2014. A total of 1311 children in pediatric anesthesia (experimental group: 649; control group: 662) were considered in the meta-analysis. The studies' sample sizes were between 38 and 247, and average age was between 2. 0 and 10. 7 years old. Study design was randomised controlled trial (RCT). Two study Jadad score were reach 4 scores (Table 2), five studies were reach 3 scores, and five studies were reach 2 scores.

Overall e ff ects of p ostoperative extubation time (min)

The summary of the meta-analysis for postoperative extubation time between experimental group and control group is shown in Table 3. There were 4 separate studies (5 comparisons) consisting of 298 children in pediatric anesthesia (experimental group: 149; control group: 149) been analyzed in the meta-analysis. The heterogeneity test showed that there were heterogeneities between studies ($Q^2 = 94. 4$, $I^2 = 96. 0\%$, $P < 0. 1$), so we used the random effects model to compare postoperative extubation time between these two groups. The overall meta-analysis showed that there were significant differences ($WMD = -3. 87$, 95% $CI = -6. 14$ to $-1. 60$, $P < 0. 01$) in patients between the two groups, suggesting that postoperative extubation time of pediatric anesthesia children in experimental group may be lower than control group.

Overall e ff ects of e ye opening time (min)

The summary of the meta-analysis for eye opening time between experimental group and control group is shown in Table 3. There were 2 separate studies consisting of 236 children in pediatric anesthesia (experimental group: 118; control group: 118) been analyzed in the meta-analysis. The heterogeneity test showed that there were no heterogeneities between studies ($Q^2 = 0.36$, $I^2 = 0.84\%$, $P > 0.1$), so we used the fixed effects model to compare eye opening time between these two groups. The overall meta-analysis showed that there were no significant differences ($WMD = -1.11$, 95% $CI = -1.49$ to -0.72, $P > 0.05$) in patients between the two groups, suggesting that eye opening time of pediatric anesthesia children in experimental group may be lower than control group.

Overall e ff ects of awakening time (min)

The summary of the meta-analysis for awakening time between experimental group and control group is shown in Table 3. There were 4 separate studies (5 comparisons) consisting of 542 children in pediatric anesthesia (experimental group: 271; control group: 271) been analyzed in the meta-analysis. The heterogeneity test showed that there were no heterogeneities between studies ($Q^2 = 5.49$, $I^2 = 27.0\%$, $P > 0.1$), so we used the fiixed effects model to compare awakening time between these two groups. The overall meta-analysis showed that there were significant differences ($WMD = -4.27$, 95% $CI = -5.28$ to -3.26, $P < 0.01$) in patients between the two groups, suggesting that awakening time of pediatric anesthesia children in experimental group may be lower than control group.

Overall e ff ects of d ischarge from the recovery room

The summary of the meta-analysis for discharge from the recovery room between experimental group and control group is shown in Table 3. There were 5 separate studies (6 comparisons) consisting of 346 children in pediatric anesthesia (experimental group: 173; control group: 173) been analyzed in the meta-analysis. The heterogeneity test showed that there were no heterogeneities between studies ($Q^2 = 2.08$, $I^2 = 0\%$, $P > 0.1$), so we used the fixed effects model to compare discharge from the recovery room between these two groups. The overall meta-analysis showed that there were no significant differences ($WMD = -1.92$, 95% $CI = -5.83$ to 1.99, $P > 0.05$) in patients between the two groups, suggesting that discharge from the recovery room of pediatric anesthesia children in experimental group may be equal to control group.

Overall e ff ects of Oculocardiac reflex (OCR)

The summary of the meta-analysis for OCR between experimental group and control group is shown in Table 3. There were 2 separate studies (3 comparisons) consisting of 374 children in pediatric anesthesia (experimental group: 181; control group: 193) been analyzed in the meta-analysis. The heterogeneity test showed that there were no heterogeneities between studies ($Q^2 = 0.74$, $I^2 = 0\%$, $P > 0.1$), so we used the fixed effects model to compare OCR between these two groups. The overall meta-analysis showed that there were no significant differences ($RR = 1.03$, 95% $CI = 0.75$ to 1.40, $P > 0.05$) in patients between the two groups, suggesting that OCR of pediatric anesthesia children in experimental group may be equal to control group.

Overall e ff ects of a gitation

The summary of the meta-analysis for agitation between experimental group and control group is shown in Table 3. There were 5 separate studies (6 comparisons) consisting of 444 children in pediatric anesthesia (experimental group: 222; control group: 222) been analyzed in the meta-analysis. The heterogeneity test showed that there were no heterogeneities between studies ($Q^2 = 5.26$, $I^2 = 0\%$, $P > 0.1$), so we used the fixed effects model to compare agitation between these two groups. The overall meta-analysis showed that there were significant differences ($RR = 1.44$, 95% $CI = 1.05$ to 1.96, $P < 0.05$) in patients between the two groups, suggesting that agitation of pediatric anesthesia children in experimental group may higher than control group.

Overall e ff ects of n ausea and vomiting

The summary of the meta-analysis for nausea and vomiting between experimental group and control group is shown in Table 3. There were 7 separate studies (8 comparisons) consisting of 514 children in pediatric anesthesia (experimental group: 257; control group: 257) been analyzed in the meta-analysis. The heterogeneity test showed that there were no heterogeneities between studies ($Q^2 = 5.43$, $I^2 = 0.49\%$, $P > 0.1$), so we used the fixed effects model to compare nausea and vomiting between these two groups. The overall meta-analysis showed that there were significant differences ($RR = 1.12$, 95% $CI = 0.78$ to 1.62, $P > 0.05$) in patients between the two groups, suggesting that nausea and vomiting of pediatric anesthesia children in experimental group may be equal to control group.

Overall e ff ects of s evere pain

The summary of the meta-analysis for severe pain between experimental group and control group is shown in Table 3. There were 2 separate studies (3 comparisons) consisting of 220 children in pediatric anesthesia (experimental group: 110; control group: 110) been analyzed in the meta-analysis. The heterogeneity test showed that there were no heterogeneities between studies ($Q^2 = 0.63$, $I^2 = 0\%$, $P > 0.1$), so we used the fixed effects model to compare severe pain between these two groups. The overall meta-analysis showed that there were significant differences ($RR = 0.95$, 95% $CI = 0.68$ to 1.33, $P > 0.05$) in patients between the two groups, suggesting that severe pain of pediatric anesthesia children in experimental group may be equal to control group.

Evaluation of publication bias analysis

The Egger’s linear regression test in Table 3 showed that there were no publication bias existing in our study ($P > 0.05$) except postoperative extubation time and awakening time

Discussion

Many studies have reported the effect with desflurane versus sevoflurane in pediatric anesthesia [8-10, 19, 21]. However, these studies have shown mixed results due to small sample sizes or low statistical power. Thus, we combined 9 studies which including 1047 children in pediatric anesthesia (experimental group: 517; control group: 530) were performed in the meta-analysis.

Our study found that postoperative extubation time and awakening time of pediatric anesthesia in experimental group may be lower than control group, agitation of pediatric anesthesia in experimental group may be higher than control group. The future of pediatric anesthesia can be thought of in terms of what will happen to the practice of anesthesia, or what will happen to the profession of pediatric anesthesia [24]. Emergence agitation has been documented as a common side-effect of sevoflurane anesthesia [25]. Repetitive sedation/anesthesia (S/A) for children receiving fractionated radiation therapy requires induction and recovery daily for several weeks [26]. Postoperative nausea and vomiting (PONV) has a high incidence in children and requires prophylactic and therapeutic strategies [27]. Pediatricians play a key role in helping prepare patients and families for anesthesia and surgery [28].

Some limitations of this study should be discussed. Firstly, signiï¬cant between-study heterogeneities were detected in the current meta-analysis, which may distort the meta-analysis. The degree of heterogeneity is one of the major concerns in meta-analysis for the validity [29], as non-homogeneous data are liable to result in misleading results. In addition, causes of the sample size of some recruited studies were small (nine), there was still need for more and high-quality RCTs to test and verify the results of this meta-analysis. Therefore, we minimized the likelihood of bias by developing a detailed protocol before initiating the study, and performed a meticulous search for published studies and used explicit methods for study selection, data extraction and data analysis.

Conclusions

Our study suggested that postoperative extubation time and awakening time of pediatric anesthesia in experimental group may be lower than control group, agitation of pediatric anesthesia in experimental group may be higher than control group.