European Review for Medical and Pharmacological Sciences 2020; 24: 11315-11322

Anesthetic effect and safety of sevoflurane combined with propofol in removing tracheobronchial foreign bodies in children

Y.-S. SONG[1], Z.-Z. YANG[1], Y.-B. HAO[1], W.-W. LIU[1], S.-S. ZHANG[1], P. WANG[1], T.-L. FAN[2], Y. ZHANG[3]

[1]Zhengzhou People's Hospital, Zhengzhou, Henan, China
[2]School of Basic Medical Sciences, Zhengzhou University, Zhengzhou, Henan, China
[3]Department of Pediatrics, The First Affiliated Hospital of Henan University of Chinese Medicine, Zhengzhou, China

Abstract. – OBJECTIVE: To systematically evaluate the anesthetic effect and safety of sevoflurane combined with propofol in removing tracheal foreign bodies in children.

MATERIALS AND METHODS: PubMed, EMbase, The Cochrane Library, China Biomedicine Database, China National Knowledge Internet, WanFang Data, and VIP databases were searched. Randomized controlled trials (RCTs) of sevoflurane combined with propofol for anesthesia during tracheal foreign body extraction in children were collected. The retrieval time was from the establishment of the database to April 10, 2019. RevMan 5.3 software was used for meta-analysis after two researchers independently screened the literature, extracted data, and evaluated the risk bias included in the study.

RESULTS: Seven RCTs involving 473 patients were included. Meta-analysis showed that the time of loss of consciousness significantly reduced (MD=-38.27, 95% CI (-41.77, -34.77), $p < 0.00001$) and the recovery time significantly reduced (MD=-12.29, 95% CI (-2.77, -1.80), $p < 0.00001$) in the sevoflurane combined with propofol group compared with the control group. In terms of safety, the heart rate was slower [MD=-11.00, 95% CI (-21.64, -0.36), $p=0.04 < 0.05$] and the incidence of cough and breath holding was lower [MD=0.38, 95% CI (0.19, 0.78), $p=0.008$] in the sevoflurane combined with propofol group than in the control group. However, no significant difference in respiratory rate and SPO 2 < 90% was found between the two groups ($p > 0.05$).

CONCLUSIONS: Sevoflurane combined with propofol is worth popularizing because of its high anesthetic effect and safety in the removal of tracheal foreign bodies in children. However, given the limited quantity and quality of the included studies, the above conclusions need to be verified by high-quality studies.

Key Words:
Propofol, Sevoflurane, Children, Tracheal foreign body, Meta-analysis, Randomized controlled study.

Introduction

A highly efficient, fast, and safe anesthesia method is highly important in removing tracheobronchial foreign bodies in children. In recent years, pediatric anesthesiologists have begun to adopt the combined use of sevoflurane and propofol as an anesthesia inducer in removing tracheobronchial foreign bodies in children[1,2]. However, a systematic assessment on the effectiveness and safety of the sevoflurane-propofol combination has yet to be reported. In the present study, the effectiveness and safety of the sevoflurane-propofol combination were evaluated objectively by performing a meta-analysis. Results are reported as follows.

Materials and Methods

Inclusion and Exclusion Criteria

Research type: the sevoflurane-propofol combined anesthesia was applied to the randomized controlled trial (RCT) study of removing tracheobronchial foreign bodies.

Research objects: children who require removing tracheobronchial foreign bodies in clinics were selected.

Intervention measures: test group: Sevoflurane and propofol were inhaled for anesthesia. The

Corresponding Authors: Tianli Fan, MD; e-mail: fantianli@zzu.edu.cn;
Zhang Yan, MD; e-mail: zhangyan6905@126.com

control group adopted the anesthesia method other than those adopted in the test group. Drug dosages were not limited in the control and test groups.

Outcome indexes: main indexes included time for loss of consciousness, wake-up time, change of heart rate at rear mirror check, and change of breaths at rear mirror check. Secondary indexes included number of cases with cough and holding breath, and number of cases with SPO_2<90%.

Exclusion criteria: (1) republished articles, (2) no available data, and (3) no acquisition of full text even by contacting the author.

Literature Review Strategy

The China National Knowledge Internet (CNKI), VIP, Wanfang Database, China Biomedicine Database (CBM), PubMed, EMbase, and The Cochrane Library were searched for RCTs about removing tracheobronchial foreign bodies in children under sevoflurane-propofol combined anesthesia from the foundation of the databases to April 1st, 2019. References included in the study were retrieved manually to supplement and acquire relevant studies. Search words in Chinese include "Tracheal foreign body," "child," "sevoflurane," and "propofol," and search words in English include "foreign," "body," "child," "infant," "adolescent," "propofol," "sevoflurane." Taking PubMed for example, the searching strategies are listed in Box 1.

```
#1. Foreign
#2. Body
#3. child
#4. infant
#5. adolescent
#6. #3 OR #4 OR #5
#7. sevoflurane
#8. propofol
#9. #1 AND #2 AND #6 AND #7 AND #8
```

Box 1. Searching strategies of PubMed.

Literature Screening and Data Selection

Two researchers were invited to screen studies and extract data independently. Any dispute was solved by discussion or consultation with the third researcher. During literature screening, titles and abstracts of articles were first read to eliminate significantly unrelated articles. Then, the whole text was read for further screening. Information was acquired by contacting the original author through telephone and e-mails if necessary. Data extraction contents include the following: (1) basic information included in the study, such as time of publishing, research title, the first author, and journal of publishing; (2) baseline features and intervention measures of research objects; (3) outcome indexes and result measurement data; and (4) key factors for deviation risk assessment.

Deviation Risk Evaluation of Included Studies

Two researchers were invited to assess deviation risks of included studies independently and check assessment results mutually. Random method, distribution hiding, blind method application, integrity of outcome data, selective report research results, and other deviation risks that were included into studies for deviation risk evaluation were assessed by Jadad. Scoring details include the following: (1) generation of random sequences: properly-2, unclear-1, and improperly -0. (2) Blinding method application: properly-2, unclear- 1, and improperly -0. (3) Withdraw: description -1 and non-description – 0. The total score was 1-5, where 1-2 indicated low-quality studies and 3-5 scores indicated high-quality studies. In accordance with the Jadad scale, RCTs with Jadad $\geq$ 2 scores were included in the meta-analysis.

Statistical Analysis

Statistical analysis was implemented using RevMan 5.3 software. The measurement data applied the mean difference (MD) as the effect analysis statistics, and the dichotomy variables chose the risk ratio (RR) as the effect analysis statistics. All effect variables provide 95% CI. First, the assessment heterogeneity of included studies was checked by χ^2-test and I^2-test. In the absence of heterogeneity (p>0.1 and I^2<50%), the fixed-effect model was used; otherwise, the random-effect model was used. Statistical significance was considered at p<0.05.

Results

Literature Retrieval Results

A total of 95 studies were retrieved preliminarily. After screening layer by layer, seven RCTs involving 373 cases of removing tracheobronchial foreign bodies in children were included[2-7]. Among these 373 cases, 190 were included in the test group (sevoflurane-propofol combination) and 183 were included in the control group. Literature retrieval process and results are shown in Figure 1.

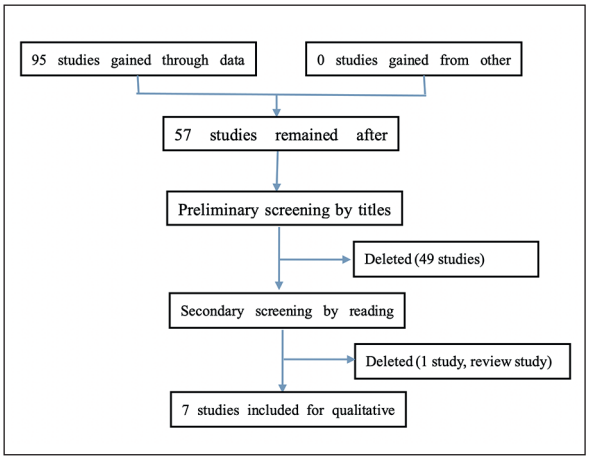

Figure 1. Literature screening process and results. *The databases searched and the number of references checked are as follows: PubMed (n=3), EMbase (n=13), The Cochrane Library (n=3), CBM (n=21), CNKI (n=33), VIP (n=22) WanFang Data (n=16), VIP (n=6).

Basic Characteristics of Included Studies

Details are listed in Table I.

Deviation Risk Evaluation Results of Included Studies

Results are listed in Table II.

Table I. Basic characteristics of included studies.

Included studies	Number of cases (T/C)	Age/year (month) (T/C)	Body weight/kg	Intervention measures		Outcome indexes
				T	C	
Qilin Liu 2012	19/19	6 months-3 years old	7-16	Inhaling 6%-8% sevoflurane+ 1-2 mg/kg	5 mg/kg ketamine im+1-2 mg/kg ketamine iv propofol iv	(2)(3)(4)
Sihai Zhou 2012	65/58	21.05 ± 3.6 /20.92 ± 8.1	18.01 ± 3.4/ 17.65 ± 2.7 (months)	Inhaling 6%-8% sevoflurane+	2-3 mg/kg propofol iv 2-3 mg/kg propofol iv	(1)(2)(5)(6)
Lihua Fang 2009	23/23	8 months-9 years old	6-29	Inhaling 6% sevoflurane+ 2.0-2.5 mg/kg iv	Propofol 2.0-2.5 mg/kg propofol 3 μg/kg iv	(1)(2)(3)(5)(6) iv+ fentanyl
Jianhui Li 2012	14/14	10 months-10 years old	7-33	Inhaling 6% sevoflurane+ propofol 2.0-2.5 mg/kg iv	Propofol 2.0-2.5 mg/kg+ fentany 3 μg/kg iv	(1)(2)(3)
Yazhe Wang 2018	22/22	3. 24 ± 1.33/ 3. 21 ± 1.22 (years old)	15.25 ± 5. 35/ 15.21 ± 5. 56	Inhaling 8% sevoflurane+ 2.5 mg/kg propofol iv	Inhaling 8% sevoflurane+. 5 μg/kg+ fentanyl iv	(1)(2)(3)(4)
Dongqin Nie 2017	19/19	6.1 ± 2.5/ 5.6 ± 2.3 (years old)	20.8 ± 3.9/ 19.6 3.3	Inhaling sevoflurane+ 2.0-2.5 mg/kg propofol iv	Inhaling sevoflurane+ 3 μg/kg fentanyl iv	(1)(2)(3)(4)
Houming Zhang 2015	28/28	6.2 ± 2.5/ 5.6 ± 2.3	20.8 ± 3.9/ 19.6 ± 3.3	Inhaling sevoflurane+2-2.5 mg/kg propofol iv	2-2.5 mg/kg propofol+3 μg/kg+ fentanyl iv	(1)(2)(3)(4)

(1) Time of loss of consciousness, (2) wake-up time, (3) changes of heart rate at ear mirror check, (4) changes of breathes at ear mirror check, (5) occurrence rate with SPO_2 < 90% at ear mirror check, and (6) occurrence rate of cough and holding breath at ear mirror check.

Table II. Deviation risk evaluation results of included studies.

Including studies	Random method	Blinding method		Outcome evaluators	Integrity of outcome data	Selective research report results	Other deviation sources	Jadad scores
		Distribution hiding	Researchers and respondents					
Qilin Liu 2012	Random number table	Unclear	Unclear	Unclear	Integrity	None	Unclear	3
Sihai Zhou 2012	Unclear	Unclear	Unclear	Unclear	Integrity	None	Unclear	2
Lihua Fang 2009	Unclear	Unclear	Unclear	Unclear	Integrity	None	Unclear	3
Jianhui Li 2012	Unclear	Unclear	Unclear	Unclear	Integrity	None	Unclear	2
Yazhe Wang 2018	Unclear	Unclear	Unclear	Unclear	Integrity	None	Unclear	2
Dongqin Nie 2017	Random number table	Unclear	Unclear	Unclear	Integrity	None	Unclear	3
Houming Zhang 2015	Random number table	Unclear	Unclear	Unclear	Integrity	None	Unclear	3

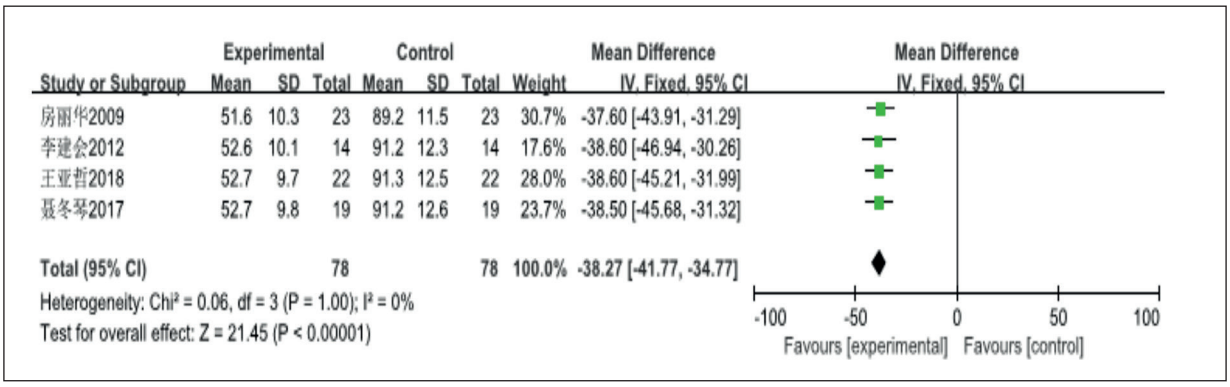

Figure 2. Meta-analysis of time of loss of consciousness in the test and control groups.

Results of Meta-Analysis

Time of Loss of Consciousness

Four RCTs were included to describe the time of loss of consciousness after anesthesia. No heterogeneity was found among different studies. In specific, 78 cases of the sevoflurane-propofol combination test group and 78 cases of the control group were covered. The meta-analysis results of the fixed-effect model showed that the children in the test group lost consciousness significantly faster than those in the control group [MD=-38.27, 95% CI (-41.77, -34.77), p<0.00001] (Figure 2).

Wake-up Time

Five RCTs were included to describe the wake-up time of children after the operation, and no heterogeneity was found among the studies. The test group included 106 cases, and the control group included 106 cases. The meta-analysis results of the fixed-effect model showed that the children in the test group wake up significantly earlier than those in the control group [MD=-12.29, 95% CI (-2.77, -1.80), p<0.00001] (Figure 3).

Changes of Breaths at Ear Mirror Check

Four RCTs were included to describe changes of breaths at ear mirror check. No heterogeneity was found among different studies. In specific, 88 cases of the sevoflurane–propofol combination test group and 88 cases of the control group were covered. The meta-analysis results of the fixed-effect model showed no statistical difference between the test and control groups [MD=0.40, 95% CI (-0.99, 1.78), p=0.57>0.05] (Figure 4).

Changes of Heart Rate at Ear Mirror Check

Six RCTs were included to describe changes of heart rate at ear mirror check. Heterogeneity was found among different studies (p<0.00001, I^2=89%). In specific, 125 cases of the sevoflu-

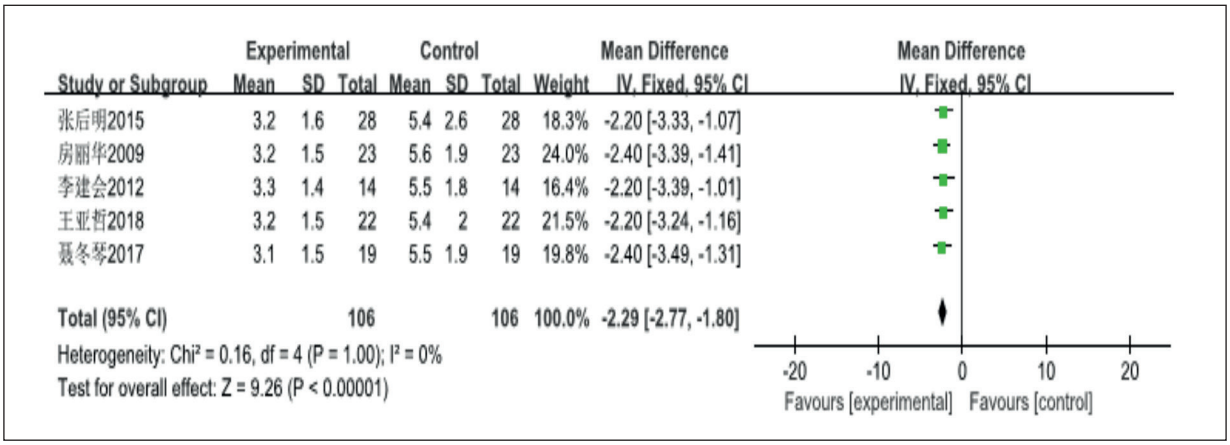

Figure 3. Meta-analysis on wake-up time of the test and control groups.

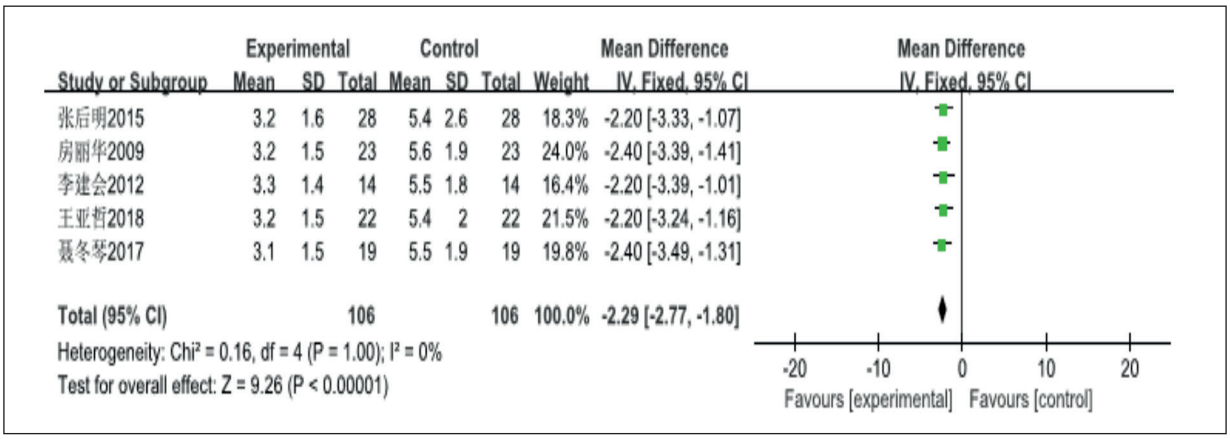

Figure 4. Meta-analysis of changes of breaths at ear mirror check between the test and control groups.

rane–propofol combination test group and 125 cases of the control group were covered. The meta-analysis results of the fixed-effect model showed statistical differences between the test and control groups with respect to changes of heart rate [MD=-11.00, 95% CI (-21.64, -0.36), p=0.04<0.05] (Figure 5).

Occurrences With SPO_2<90% at Ear Mirror Check

Two RCTs were included to describe occurrences with SPO_2<90% at ear mirror check. No heterogeneity was found among different studies. In specific, 88 cases of the sevoflurane–propofol combination test group and 81 cases of the control group were covered. The meta-analysis results of the fixed-effect model showed that the test and control groups had statistical differences compared with None with respect to occurrences with SPO_2<90% at ear mirror check [MD=0.45, 95% CI (0.20, 1.03), p=0.06] (Figure 6).

Occurrences of Cough and Holding Breath at Ear Mirror Check

Two RCTs were included to describe the occurrences of cough and holding breath at ear mirror check. No heterogeneity was found among different studies. In specific, 88 cases of the sevoflurane–propofol combination test group and 81 cases of the control group were covered. The meta-analysis results of the fixed-effect model showed that the test group had lower occurrences of cough and holding breath than the control group, showing statistical difference [MD=0.38, 95% CI (0.19, 0.78), p=0.008] (Figure 7).

Discussion

Foreign bodies in the bronchus attack young children, especially infants less than 3 years old, accounting for about 70%-80% of total cases. Anesthesia performance determines the success

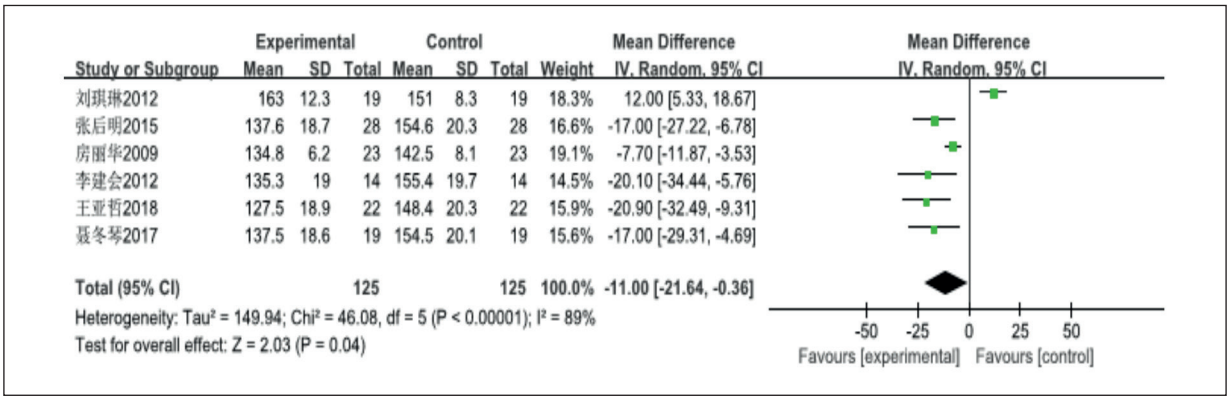

Figure 5. Meta-analysis of changes of heart rate at ear mirror check between the test and control groups

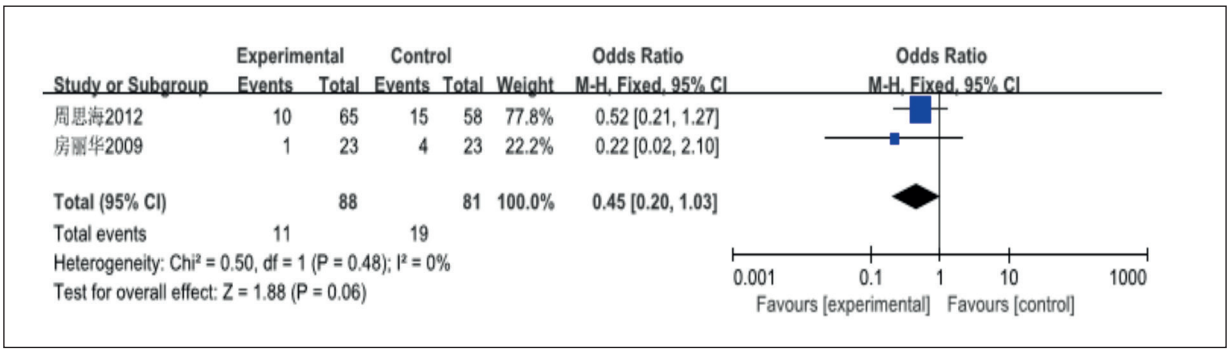

Figure 6. Meta-analysis of occurrences with SPO_2<90% at ear mirror check between the test and control groups.

of operation. Due to the uniqueness of children patients, complications such as laryngospasm, holding breath, and SPO_2 reduction commonly occur during the operation[8-13]. Therefore, precautions should be taken in the selection of anesthesia and drugs.

At present, experts have a consensus on inhalation anesthesia of sevoflurane, dexmedetomidine, or remifentanil + propofol for removing tracheobronchial foreign bodies in children. However, these anesthesia modes are unsatisfying in loss of consciousness, wake-up time after operation, and complications in operation (e.g., cough and holding breath). In clinics, inhalation of sevoflurane combined with intravenous injection of propofol contributes satisfying anesthesia in removing tracheobronchial foreign bodies in children. A meta-analysis on included studies concluded that inhalation of sevoflurane combined with intravenous injection of propofol takes shorter time of anesthesia compared with other methods, showing statistical differences (p<0.05), indicating its clinical effectiveness and reliability. This result might be related to the clinical pharmacological characteristics of propofol and sevoflurane, such as strong anesthesia, rapid onset, short duration, and early wake-up. With respect to anesthesia safety evaluation, meta-analysis of relevant studies showed that inhalation of sevoflurane combined with intravenous injection of propofol brings relatively lower heart rate at ear mirror check than other anesthesia methods, accompanied with the lower occurrence of cough and holding breath. The safety of the proposed anesthesia is statistically verified (p<0.05). However, the proposed anesthesia method shows no statistical difference with None in terms of changes of breaths at ear mirror check and occurrence of SPO_2<90% (p>0.05). This result might be related to the relatively small sample size. This study has some limitations. First, the overall quality of included studies is relatively low. Only three studies had Jadad scores =3; the remaining studies had Jadad scores =2. The large deviation risks deteriorate the reliability of conclusion. Second, only few studies were included, which resulted in the unsatisfactory efficiency of statistics. Third, the intervention measures of control groups in

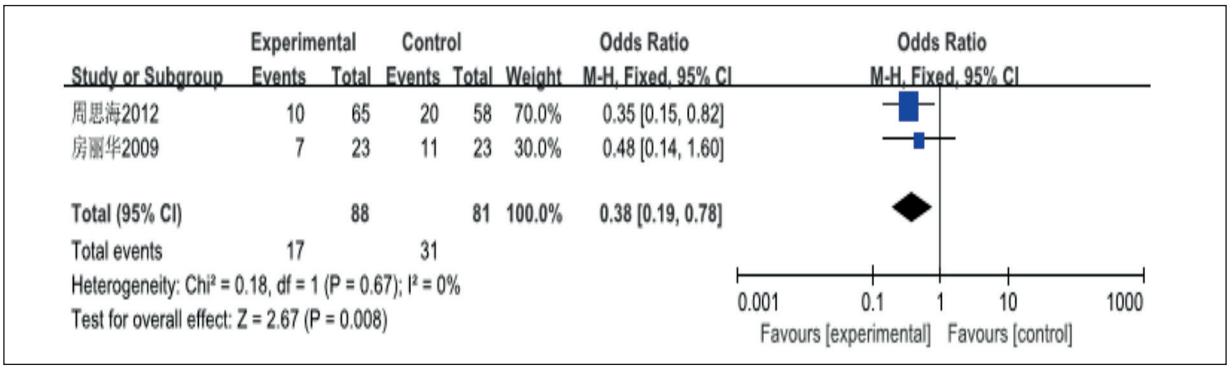

Figure 7. Meta-analysis of occurrences of cough and holding breathes at ear mirror check between the test and control groups.

different groups varied, and clinical heterogeneity was found in drug administration. These phenomena might cause certain unreliability of the results.

Conclusions

In sum, inhalation of sevoflurane combined with intravenous injection of propofol provides reliable and safe anesthesia in removing tracheobronchial foreign bodies in children and possesses outstanding values of clinical promotion. Given the limited quality of included studies, relevant problems in the above conclusions must be answered by designing a large-scale, multi-center RCT.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Zhang XT, Qi DS, Liu HC, Su EZ, Li J. Propofol target controlled infusion plus a low concentration of sevoflurane inhalation inductionanesthesia for the removal of foreign body from tracheobronchus in children. Zhonghua Yi Xue Za Zhi 2011; 91: 3333-3336.
2) Chai J, Wu XY. A retrospective study of anesthesia during rigid bronchoscopy for airway foreign body removal in children: propofol and sevoflurane with spontaneous ventilation. Paediatr Anaesth 2014; 24: 1031-1036.
3) Zhan AL, Li Q, Luo XH, Qin CM. Topical anesthesia with different dose of remifentanil and propofol intravenous anesthesia combined with inhalational sevoflurane in children having foreign-body removed from bronchus. J Southeast Univ (Med Sci Edi) 2013; 32: 162-165.
4) Zhang Q, Dong H. The Application of sevoflurane combined with propofol and fentanyl under surface anesthesia in the removal of tracheal foreign body. Shaanxi Medical Journal 2016; 45: 23-25.
5) Zhou SH, Shang ZG. Comparison of three anesthesia methods in removal of tracheal foreign bodies in children. Xinjiang Medical Science 2012; 42: 7-9.
6) Zhang J, Wang Y, Li B, Zhang W. Remifentail infusion for paediatric bronchoscopic foreign body removal: comparison of sevoflurane with propofol for anaesthesia supplementation for bronchoscope insertion. Anaesth Intensive Care 2010; 38: 905-10.
7) Liao R, Li JY, Wang ZA. Comparison of sevoflurane volatile induction/maintenance anaesthesia and propofol-remifentanil total intravenous anaesthesia for rigid bronchoscopy under spontaneous breathing for tracheal/bronchial foreign body removal in children. Eur J Anaesthesiol 2010; 27: 903-4.
8) Chen L,Yu L, Fan Y, Manyande A. A comparison between total intravenous anaesthesia using propofol plus remifentanil and volatile induction/ maintenance of anaesthesia using sevoflurane in children undergoing flexible fibreoptic bronchoscopy. Anaesth Intensive Care 2013; 41: 742-9.
9) Zhang X, Li WX, Chen YZ. Postoperative adverse respiratory events in preschool patients with inhaled foreign bodies: an analysis of 505 cases. Paediatr Anaesth 2011; 21: 1003-1008.
10) Fidkowski CW, Zheng H, Firth PG. The anesthetic considerations of tracheobronchial foreign bodies in children: a literature review of 12,979 cases. Anesth Analg 2010; 111: 1016-1025.
11) Tan HK , Brown K , McGill T , Kenna MA , Lund DP , Healy GB Airway foreign bodies (FB): a 10-year review. Int J Pediatr Otorhinolaryngol 2000; 56: 91-93.
12) Latifi X, Mustafa A, Hysenaj Q. Rigid tracheobronchoscopy in the management of airway foreign bodies: 10 years experience in Kosovo. Int J Pediatr Otorhinolaryngol 2006; 70: 2055-2059.
13) Wu X, Cao J, Shan C, Peng B, Zhang R, Cao J, Zhang F. Efficacy and safety of propofol in preventing emergence agitation after sevoflurane anesthesia for children. Exp Ther Med 2019; 17: 3136-3140.