Review Article
Comparison of the anesthetic effect of sufentanil versus fentanyl in pediatric surgical patients: a meta-analysis

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Abstract: Objective: To evaluate the anesthetic effects of sufentanil and fentanyl in pediatric surgery. Methods: We conducted a comprehensive search across multiple databases, including Wanfang, CNKI, Chinese Biomedical Literature, VIP, Embase, PubMed, Cochrane Library, and Web of Science. Studies were retrieved to screen randomized controlled trials (RCTs) comparing sufentanil and fentanyl use in children during surgery. Primary outcomes included mean arterial pressure (MAP), heart rate (HR), Ramsay sedation score, and restlessness score (RS). Pooled and sensitivity analyses were performed, and risk of bias was assessed. Results: Fourteen studies compared the efficacy of sufentanil and fentanyl in terms of MAP immediately after intubation. The results demonstrated that sufentanil exhibited a more pronounced reduction in MAP compared with fentanyl (SMD: -0.62; 95% CI = [-0.97, -0.27]; I^2 = 79.6%, P < 0.001). A total of 5 studies compared the efficacy of sufentanil and fentanyl in MAP at five and fifteen minutes after intubation, with sufentanil again showing a more pronounced reduction in MAP compared with fentanyl (P < 0.05). Additionally, sufentanil resulted in a more stable HR compared to fentanyl (SMD: -0.46; 95% CI = -0.58 - -0.33; I^2 = 53.5%, P < 0.0001). There were 4 studies reporting the effects of sufentanil on RS, indicating that sufentanil led to significantly greater reductions in RS compared to fentanyl (SMD: -1.59; 95% CI = [-2.52, -0.66]; I^2 = 91.5%, P < 0.001). Conclusion: Among the children undergoing surgery, sufentanil demonstrates more advantages over fentanyl in maintaining stable hemodynamics and reducing postoperative agitation, offering better clinical benefits.

Keywords: Anesthetic effect, sufentanil, fentanyl, children, surgery, meta-analysis

Introduction

Pediatric patients are prone to preoperative emotional instability and poor cooperation, making them more susceptible to postoperative mental and behavioral disorders, such as crying and restlessness after anesthesia recovery. These issues not only increase the risk associated with surgical anesthesia but also negatively impact children's physical and mental well-being [1, 2]. Given the unique physiological and psychological characteristics of children, they frequently experience adverse emotional responses, such as fear and unfamiliarity with the surgical environment, which can heighten sympathetic nervous system activity and lead to undesirable stress reactions, potentially affecting surgical outcomes [3]. Therefore, pediatric anesthesia requires fast and stable onset, while minimizing the impact on the respiratory and circulatory systems' normal physiological functions [4]. Strengthening anesthesia management and selecting appropriate anesthetic drugs are therefore essential in pediatric surgical care.

Opioid drugs, a type of potent narcotic analgesics with strong central analgesic effects, are widely used in clinical practice [5]. Fentanyl and its derivatives, as representative drugs, offer advantages such as stable circulation and strong analgesic effect [6, 7]. Sufentanil, a fentanyl derivative, has an analgesic potency 5 to 10 times greater than fentanyl, with added benefits of rapid onset, no histamine release, and stable function across multiple systems [8]. It is currently the most potent narcotic analgesic available for clinical practice. In pediatric surgi-

cal procedures, they can be used for anesthesia induction, intraoperative analgesia, and postoperative pain management [9]. There is a lack of comprehensive research comparing different analgesic strategies or combinations to determine the most suitable and safe approach for pediatric surgical patients.

Therefore, this study aims to compare the anesthetic effects and postoperative recovery between sufentanil and fentanyl in pediatric surgeries through a meta-analysis, providing a more reliable evidence-based foundation for clinical decision-making.

Methods

Data sources

Eligible publications were identified through electronic searches across several databases, including Wanfang, CNKI, Chinese Biomedical Literature, VIP, Embase, PubMed, Cochrane Library, Web of Science from their inception to June 2024. The search strategy incorporated a combination of MeSH terms and keywords: (((("sufentanil"[Mesh]) OR ((((((Sulfentanyl[Title/Abstract]) OR (Sulfentanil[Title/Abstract])) OR (Sufenta*[Title/Abstract])) AND (fentanyl[Title/Abstract])) OR (Fentanest[Title/Abstract])) OR (Fentanyl Citrate [Title/Abstract]))) AND (("Children During Surgery" [Supplementary Concept]) OR (("Pediatric surgery" [Supplementary Concept]) AND ((randomized controlled trial [Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract])). This meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD42024588193.

Inclusion and exclusion criteria of literature screening

Inclusion criteria: 1) Study type: randomized controlled trial (RCTs) or quasi-RCTs; 2) Study population: children undergoing surgery; 3) Treatment plan: comparisons involving sufentanil or fentanyl; 4) Outcome measure: At least one of the following: heart rate (HR), mean arterial pressure (MVP), blood pressure, cardiac index, central venous pressure, awakening time, extubation time, ICU stay time and Visual analogue scale (VAS) for pain; 5) Publication type: peer-reviewed article in English or Chinese.

Exclusion criteria: 1) Non-randomized controlled trial, such as a single-arm study; 2) Animal studies, case reports, or non-primary literature; 3) Studies with incomplete data, duplicate publications, review articles, literature where the original article could not be retrieved, or literature where the outcome indicator was not related to the specified conditions.

Literature screening and data extraction

Two researchers (Yanjun Ke and Liqing Gao) independently assessed the eligibility of studies based on the inclusion and exclusion criteria outlined above. Both researchers started by reviewing the titles and abstracts. If a definitive conclusion about a study's eligibility could not be drawn from the title and abstract alone, they proceeded to a full-text review. For studies meeting the inclusion criteria, the researchers conducted data selection and assessed the quality of the literature. Discrepancies regarding inclusion or exclusion were resolved through discussion or, if necessary, by consulting a third-party arbitrator.

Evaluation of literature quality

Two researchers (Yanjun Ke and Liqing Gao) evaluated the quality of the literature according to the Jadad scale [10], which includes the selection of the study population, outcome measures, and comparability between groups. Any disagreements during the evaluation process were resolved through internal group discussions.

Risk of bias assessment

Risk of bias assessment within studies was assessed for the primary outcome by two reviewers (Yanjun Ke and Liqing Gao) independently using the revised Cochrane Collaboration's Risk of Bias Tool (ROB) version 2.0 [11]. Any disagreement was resolved by consensus. Each study was classified as having a low risk of bias if all individual domains were rated as low risk. Otherwise, it was considered high risk if any domain was judged to be at high risk of bias. Studies were noted as having 'some concern' in other situations.
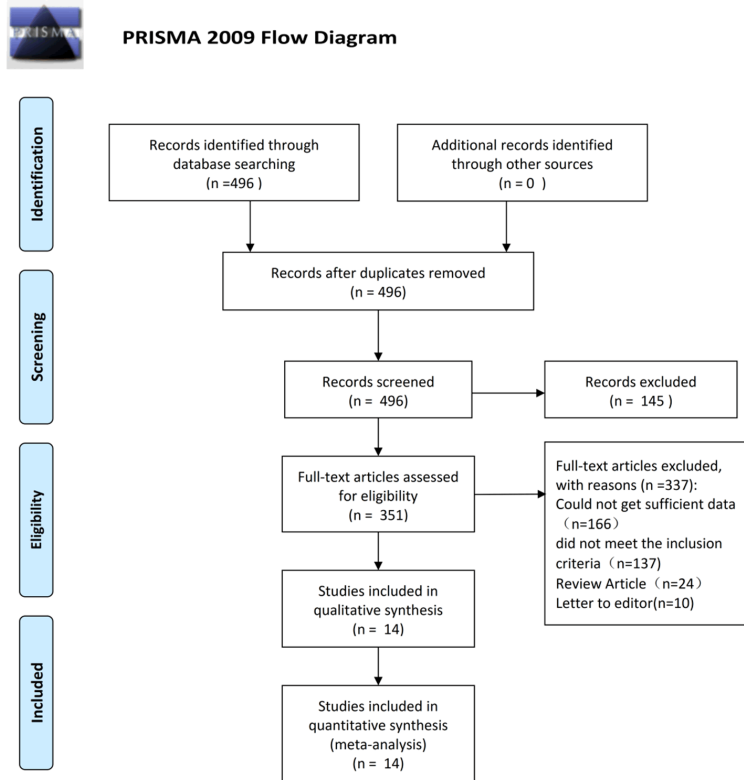
PRISMA 2009 Flow Diagram

Identification

Records identified through database searching (n = 496)

Additional records identified through other sources (n = 0)

Records after duplicates removed (n = 496)

Screening

Records screened (n = 496)

Records excluded (n = 145)

Eligibility

Full-text articles assessed for eligibility (n = 351)

Full-text articles excluded, with reasons (n = 337):
Could not get sufficient data （n=166）
did not meet the inclusion criteria （n=137）
Review Article （n=24）
Letter to editor(n=10)

Studies included in qualitative synthesis (n = 14)

Included

Studies included in quantitative synthesis (meta-analysis) (n = 14)

Figure 1. Flow diagram of the literature search process.

Statistical methods

All analyses were performed using Review Manager (RevMan 5.3, Nordic Cochrane Center, Copenhagen, Denmark) and Stata 13.1 (StataCorp, College Station, Texas). For continuous variables, weighted mean difference (WMD) and 95% confidence intervals (CI) were calculated using the inverse variance method. For studies providing only standard error (SE) data, the standard deviation (SD) was calculated using the equation $SD = SE/\sqrt{N}$ (N represents the sample size). The statistical results of clinical outcome variables were presented as a forest plot. Each effect size and its corresponding 95% CI were represented by a horizontal line, with the length of the line indicating the range of the CI. The square marker in the middle of the line represented the effect size, while the vertical line represented a WMD of 0. The diamond symbol represented the overall results of the meta-analysis. A significance level of 0.05 was used; if the short line or diamond symbol intersected with the vertical line, it indicated that the *P*-value was greater than 0.05 or

the 95% CI included 0 (WMD), suggesting that the difference was not statistically significant.

Results

Literature search and study characteristics

Out of 496 studies initially identified, 351 potentially relevant studies were extracted after exclusion of duplicates and irrelevant records. Further exclusions were made for reviews, case reports, letters, and studies that didn't meet the inclusion criteria. Finally, 14 studies [12-25] were included in the meta-analysis. The study selection process is depicted in **Figure 1**. The characteristics of the studies included are shown in **Table 1**. All of these studies were conducted in China. Randomization was performed using either a computer-generated random list or randomly generated number patterns in most of the trials [12-25]. Overall, the quality of these studies was rated as moderate to high (**Figure 2**).

Efficacy of sufentanil and fentanyl on mean arterial pressure (MAP)

Ten studies [12-15, 17-19, 21-23] compared the efficacy of sufentanil and fentanyl on MAP immediately after intubation. The results demonstrated that sufentanil exhibited a more pronounced reduction in MAP compared with fentanyl (SMD: -0.62; 95% CI = [-0.97, -0.27]; I^2 = 79.6%, P < 0.001) (**Figure 3**). A total of 4 studies [12, 14, 21, 24] compared the efficacy of sufentanil and fentanyl in MAP at one and three minutes after intubation, and the results indicated no significant difference between the two (both P > 0.05) (**Figure 3**). A total of 5 studies [12, 14, 15, 21, 24] compared the efficacy of sufentanil and fentanyl in MAP at five and fifteen minutes after intubation, and the results demonstrated that sufentanil exhibited a more

Table 1. Basic characteristics of the included literature

| First author/year	Country	Subjects (Fentanyl group/Sufentanil group)	Interventions (Fentanyl group/Sufentanil group)	NOS score	Outcome indicators	Operation
Hou 2014 [12]	China	39/39	Fentanyl group: fentanyl 3 ug/Kg Sufentanil group: sufentanil 0.3 ug/Kg	7	Systolic blood pressure, diastolic blood pressure, heart rate	Unclear
Lin 2010 [13]	China	30/26	Fentanyl group: fentanyl 5~6 ug/Kg Sufentanil group: sufentanil 0.5~0.6 ug/Kg	7	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score, agitation score	Nasopharyngeal surgery
Liu 2007 [14]	China	40/40	Fentanyl group: fentanyl 2 ug/Kg Sufentanil group: sufentanil 0.2 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate	Plastic surgery
Liu 2014 [15]	China	50/50	Fentanyl group: fentanyl 3 ug/Kg Sufentanil group: sufentanil 0.3 ug/Kg	6	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score, agitation score	Pediatric tonsillectomy
Liu 2017 [16]	China	40/40	Fentanyl group: fentanyl 2-4 ug/Kg Sufentanil group: sufentanil 0.2-0.4 ug/Kg	7	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score	Tonsillectomy and adenoidectomy
Pei 2011 [17]	China	31/32	Fentanyl group: fentanyl 4 ug/Kg Sufentanil group: sufentanil 0.5 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score, agitation score	Laparoscopic high ligation of hernia sac
Wang 2009 [18]	China	30/30	Fentanyl group: fentanyl 3 ug/Kg Sufentanil group: sufentanil 3 ug/Kg	6	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score, agitation score	Tonsillectomy and adenoidectomy
Wu 2009 [19]	China	40/40	Fentanyl group: fentanyl 3 ug/Kg Sufentanil group: sufentanil 3 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score, agitation score	Unclear
Xu 2022 [20]	China	34/34	Fentanyl group: fentanyl 5 ug/Kg Sufentanil group: sufentanil 0.5 ug/Kg	7	Systolic blood pressure, diastolic blood pressure, heart rate	3
Xue 2007 [21]	China	30/30	Fentanyl group: fentanyl 2 ug/Kg Sufentanil group: sufentanil 0.2 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate	Plastic surgery
Yang 2012 [22]	China	40/40	Fentanyl group: fentanyl 4 ug/Kg Sufentanil group: sufentanil 0.4 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score, agitation score	Pediatric tonsillectomy
Yang 2021 [23]	China	36/34	Fentanyl group: fentanyl 2 ug/Kg Sufentanil group: sufentanil 0.2 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate	Tonsillectomy and Adenotomy
Yao 2009 [24]	China	12/12	Fentanyl group: fentanyl 5 ug/Kg Sufentanil group: sufentanil 0.7 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate	surgical repair of congenital cardiac defect with cardiopulmonary bypass
Zhang 2017 [25]	China	30/30	Fentanyl group: fentanyl 1 ug/Kg Sufentanil group: sufentanil 0.1 ug/Kg	8	Systolic blood pressure, diastolic blood pressure, heart rate, sedation score, agitation score	Laparoscopic inguinal hernia repair surgery
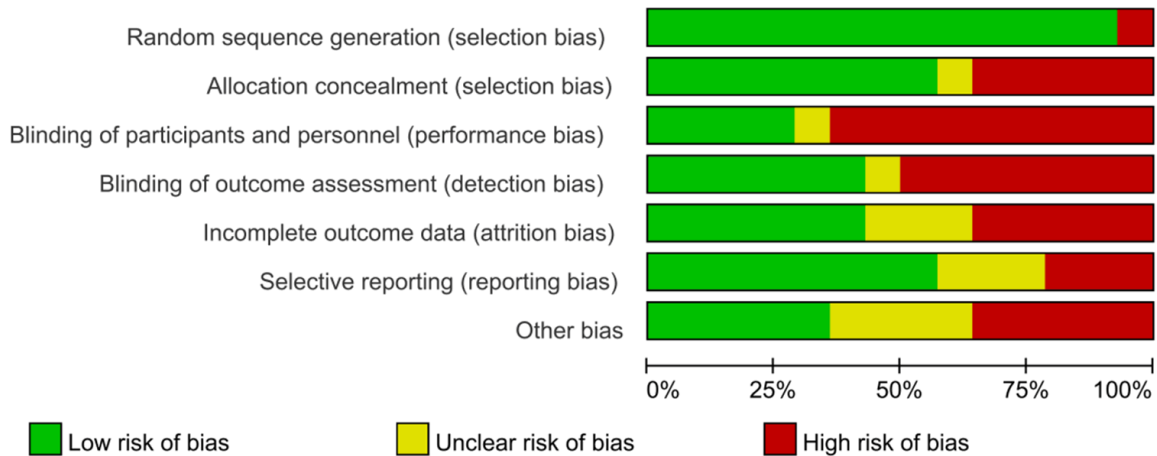
Figure 2. The assessment of risk of bias in the included studies.

pronounced reduction in MAP compared with fentanyl (both P < 0.05) (**Figure 3**). A total of 9 studies [13, 15-20, 22, 23] compared the efficacy of sufentanil and fentanyl in MAP at the end of the operation, and the results demonstrated that sufentanil exhibited a more pronounced reduction in MAP compared with fentanyl (P = 0.005) (**Figure 3**).

Efficacy of sufentanil and fentanyl on heart rate (HR)

Nine studies [12-15, 17, 18, 21-23] compared the efficacy of sufentanil and fentanyl on HR immediately after intubation. The results demonstrated that sufentanil resulted in a more stable HR compared to fentanyl (SMD: -0.48; 95% CI = -0.75 - -0.21; I^2 = 64.3%, P = 0.004) (**Figure 4**). A total of 6 studies [12, 14, 16, 20, 21, 24] compared the efficacy of sufentanil and fentanyl in HR at one minutes after intubation, and the results indicated no significant difference between the two (P = 0.156) (**Figure 4**). A total of 3 studies [12, 14, 21] compared the efficacy of sufentanil and fentanyl in HR at three minutes after intubation, and the results indicated no significant difference between the two (P = 0.398) (**Figure 4**). A total of 5 studies [12, 14, 16, 21, 24] compared the efficacy of sufentanil and fentanyl in HR at five and fifteen minutes after intubation, and the results demonstrated no significant difference between the two (P = 0.092) (**Figure 4**). At the end of the operation, sufentanil had a better HR compared to fentanyl (SMD: -0.51; 95% CI = -0.82 - -0.20; I^2 = 73.6%, P < 0.0001), and the total

results showed that sufentanil resulted in a more stable HR compared to fentanyl (SMD: -0.46; 95% CI = -0.58 - -0.33; I^2 = 53.5%, P < 0.0001) (**Figure 4**).

Efficacy of sufentanil and fentanyl on Ramsay score

Four studies [13, 15, 18, 25] reported the effects of sufentanil and fentanyl on Ramsay score, and the results showed that Ramsay scores were significantly improved in the sufentanil group (SMD = 0.03; 95% CI = [-1.74, 1.79]; P < 0.0001) (**Figure 5**).

Efficacy of sufentanil and fentanyl on restlessness score (RS)

Four studies [13, 15, 18, 25] reported the effects of sufentanil and fentanyl on RS. Compared to the fentanyl group, sufentanil resulted in more significant reductions in restlessness scores (SMD: -1.59; 95% CI = [-2.52, -0.66]; I^2 = 91.5%, P < 0.001) (**Figure 6**).

Publication bias

The funnel plots for each meta-analysis are shown in **Figure 7**. The symmetry observed in these plots, with most studies aligning near the central axis, indicates relatively low levels of publication bias.

Discussion

Due to the unique anatomical, physiological, and pharmacological characteristics of chil-

Anesthetic effect of sufentanil and fentanyl in children during surgery
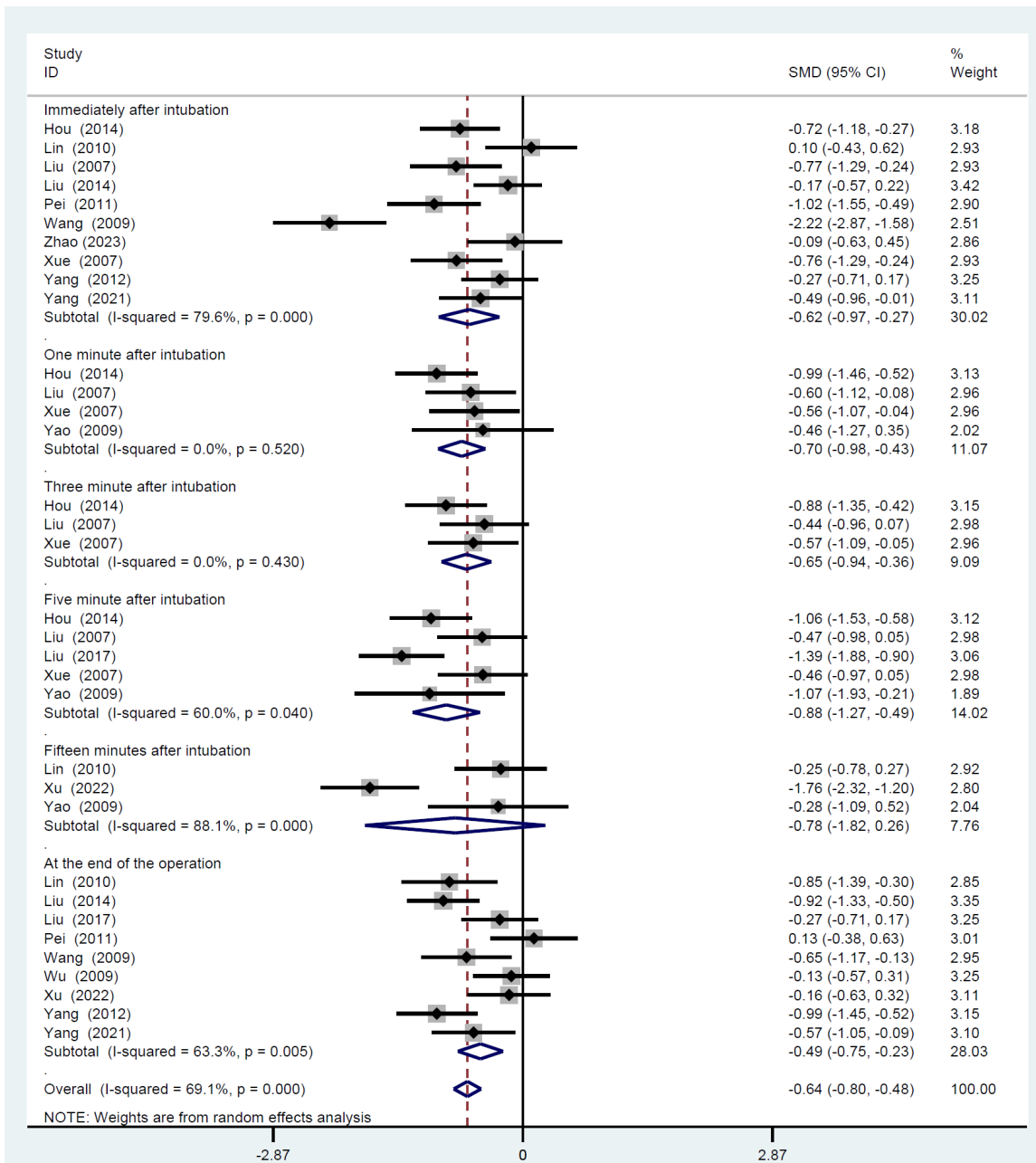

Figure 3. Forest plot for the meta-analysis of MAP. Note: MAP: mean arterial pressure.

dren, they are more sensitive to opioid drugs than adults, making the selection of the appropriate opioid drug crucial. Sufentanil, a new type of μ-opioid receptor agonist, has the strongest analgesic effect among the fentanyl family. It is 5 to 10 times more potent than fentanyl, with a slightly faster onset and shorter maintenance duration compared to fentanyl [26, 27].

In terms of mean arterial pressure (MAP), this meta-analysis demonstrated that after general anesthesia induction with sufentanil, the fluctuations in MAP were significantly smaller than that of the fentanyl group, indicating that sufentanil can better suppress the blood pressure fluctuation caused by tracheal intubation stimulation, maintain the stability of the circulatory system, and effectively suppress the intu-

Anesthetic effect of sufentanil and fentanyl in children during surgery
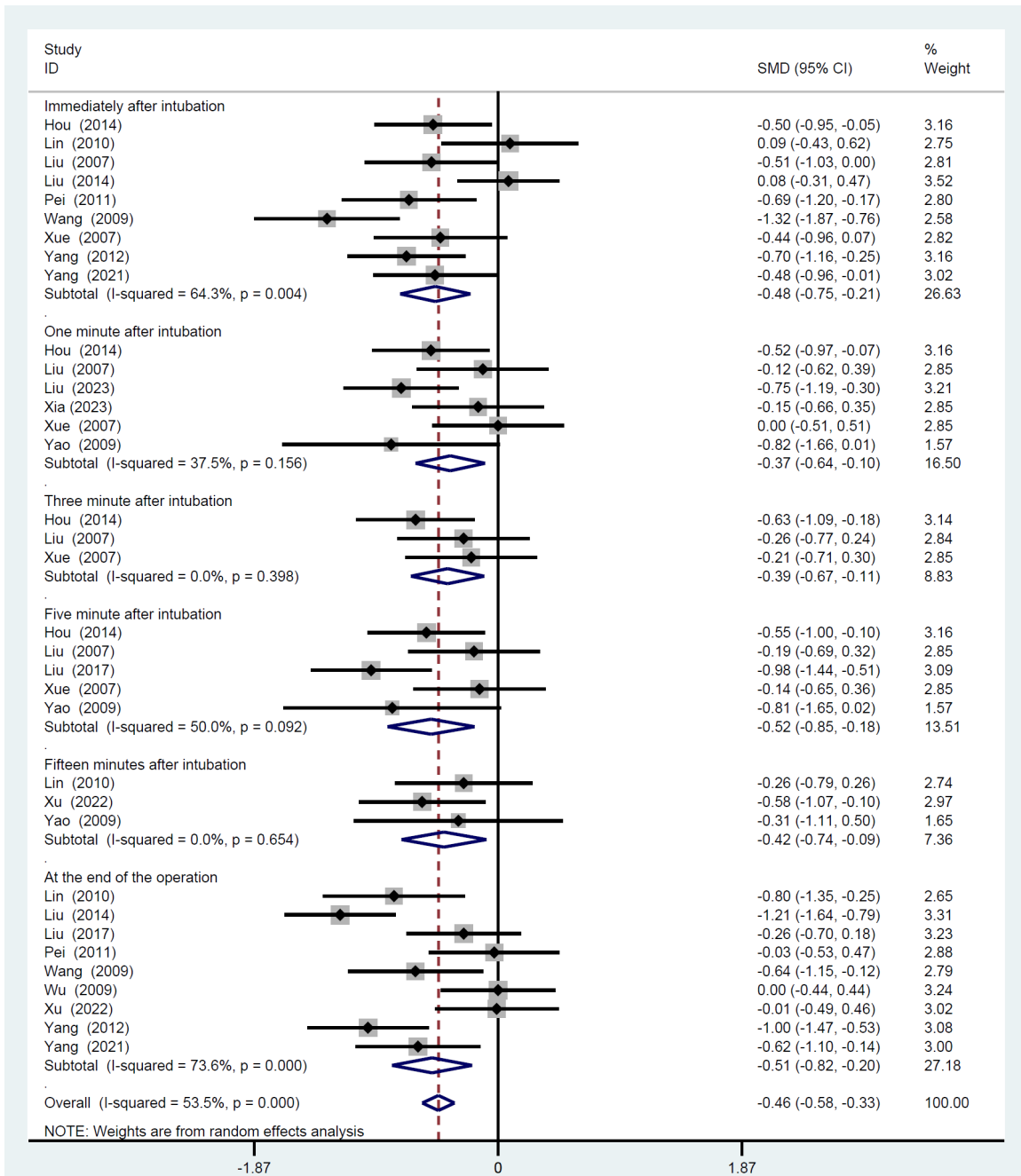

Figure 4. Forest plot for meta-analysis of HR. Note: HR: heart rate.

bation response. Sufentanil can better regulate the central nervous system's response to pain and stress, reducing the activation of the sympathetic nervous system [28]. This helps to minimize excessive increase in heart rate and blood pressure that may occur due to surgical stimulation and pain. Sufentanil also has a longer duration of action and a more stable pharmacokinetic profile, which allows for more sus-

tained and controlled analgesic effects, leading to a more gradual and controlled response in blood pressure, preventing large fluctuations [29, 30]. In addition, sufentanil is associated with a relatively lower potential for side effects, such as tachycardia and hypertension, which are commonly seen with less stable blood pressure control [31]. The precise and targeted action of sufentanil helps to create a more
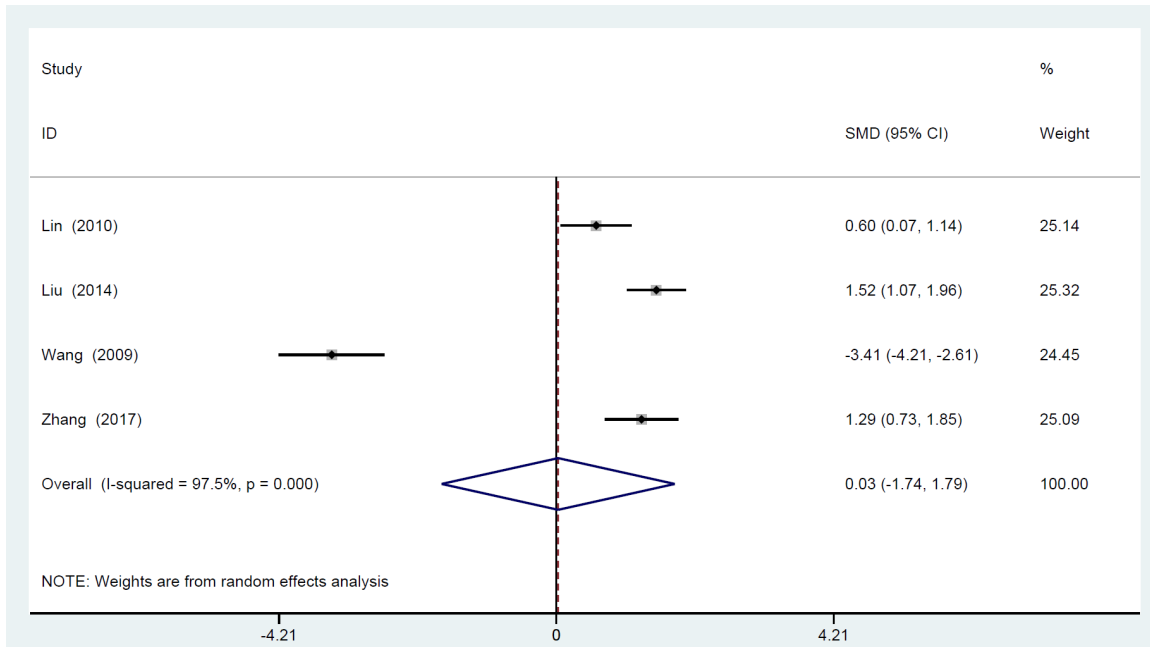
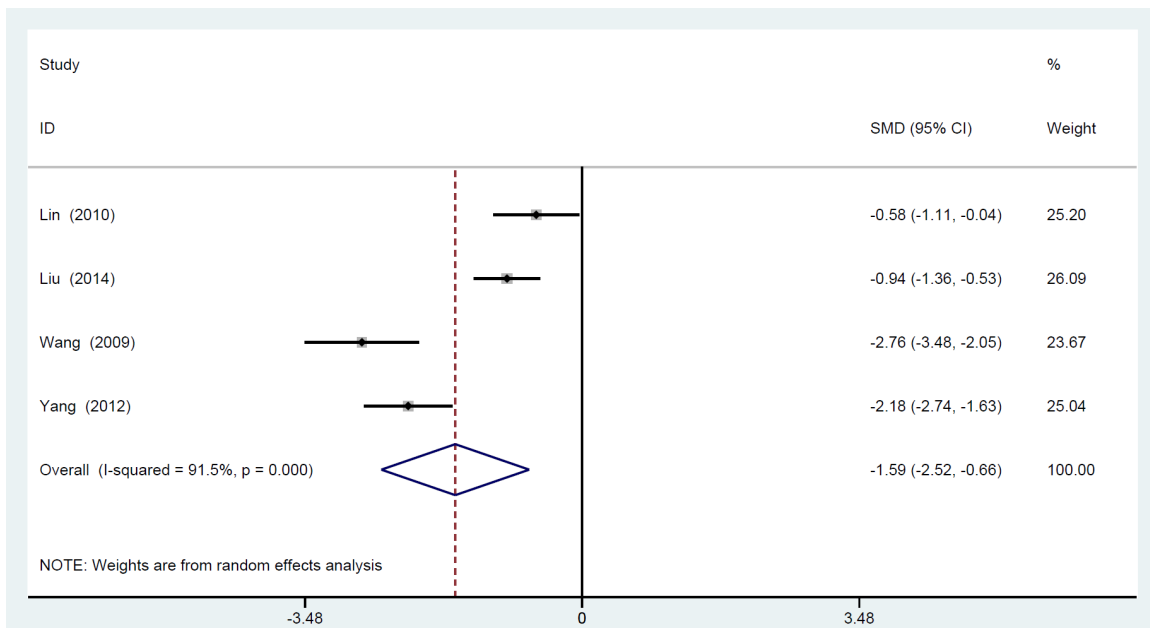**Figure 5.** Forest plot for meta-analysis of the Ramsay score.

Figure 6. Forest plot for meta-analysis of RS. Note: RS: Restlessness score.

favorable environment for maintaining stable blood pressure during pediatric surgeries, minimizing the risks and complications associated with significant blood pressure fluctuations.

This meta-analysis showed that the sedation scores of the sufentanil group during the awak-

ening period were higher than those of the fentanyl group, while the restlessness scores were lower, indicating that sufentanil enables children to restore spontaneous breathing more quickly after operation. Additionally, it retains a stronger analgesic and sedative effect, allowing children to tolerate the endotracheal tube
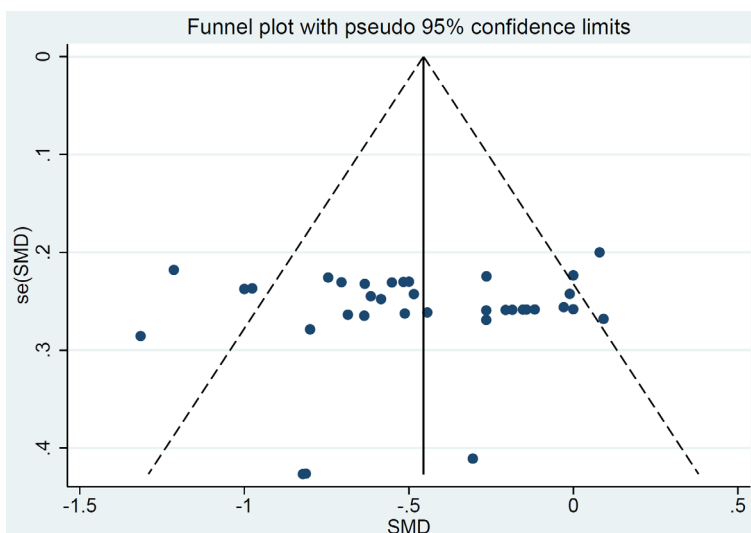
Figure 7. Publication bias analyzed using funnel plot.

better and reducing restlessness caused by pain, thereby facilitating a smoother postoperative recovery.

Firstly, sufentanil has a higher affinity for opioid receptors, which can more effectively bind to and activate these receptors, resulting in more potent sedative and analgesic actions [32]. Secondly, it can better regulate the central nervous system, helping to calm the child's body and mind, thereby minimizing restlessness [33]. Moreover, sufentanil has a more stable pharmacokinetic profile, which can provide a more sustained and controllable sedative effect, reducing fluctuations in the child's condition and subsequent restlessness [34]. Additionally, sufentanil's enhanced effect on neurotransmitter regulation contributes to maintaining a more stable mental state, further decreasing the likelihood of postoperative restlessness [35].

This meta-analysis has certain limitations. Firstly, due to the limited number of RCTs published, the number of studies included in this meta-analysis is relatively small, and currently the research data in this aspect abroad is relatively scarce. As all the included studies were conducted domestically, this analysis does not provide insights into foreign patient populations. Secondly, many of the 14 studies included had small sample sizes, resulting in a relatively small overall sample size, which may increase random errors and affect the accura-

cy of the confidence interval. Thirdly, there were variations in the doses of sufentanil and fentanyl used across the studies, complicating the analysis of the results. Finally, there were relatively few studies investigating adverse reactions, preventing a secondary analysis of the adverse reactions. Therefore, larger, multi-center, and high-quality RCTs are needed for further verification of these findings.

Conclusion

In children undergoing surgery, sufentanil has more advantages over fentanyl in maintaining stable hemodynamics and reducing postoperative agitation, leading to better clinical outcomes. However, given the limitations in the included population, sample size and measured indicators in this study, further randomized controlled trials are still necessary to confirm these results.

Disclosure of conflict of interest

None.

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