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Original Contribution

Effect and safety of propofol for sedation during colonoscopy: A meta-analysis

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ABSTRACT

Study objectives: The study is to compare the efficacy and safety of propofol with traditional sedation agents for sedation during colonoscopy.
Design: Meta-analysis.
Setting: China-Japan Union Hospital of Jilin University.
Measurements: We conducted a comprehensive literature search through the database of Pubmed, Embase, and Web of Science. The continuous outcomes were expressed with weight mean difference (WMD) or standardized mean difference (SMD) with 95% confidence interval (95%CI); and dichotomous outcomes were expressed with risk ratio (RR) with 95%CI. A fixed-effect model or random-effect model was used to pool the estimate according to the heterogeneity across included studies.
Main results: Nineteen studies involving 2512 patients were included in this study. Compared with traditional sedation agents, propofol had better effects in the recovery time (WMD = −5.94 min, 95%CI: −9.24, −2.63; P < 0.001), discharge time (WMD = −33.57 min, 95%CI: −71.73, −4.60; P = 0.015), satisfaction score (SMD = 0.73, 95%CI: 0.13, 1.33; P = 0.017), time to sedation (WMD = −4.31 min, 95%CI: −4.93, −3.69; P < 0.001), and time to ambulation (WMD = −27.20 min, 95%CI: −29.84, −24.56; P < 0.001). Moreover, propofol had comparable effects with traditional sedation agents in terms of other outcomes, including procedure time (WMD = −0.38 min, 95%CI: −0.84, 0.08; P = 0.108), pain score (SMD = 0.22, 95%CI: −0.21, 0.65; P = 0.318), amnesia rate (RR = 0.93, 95%CI: 0.78, 1.11; P = 0.431), apnea rate (RR = 0.52, 95%CI: 0.15, 1.85; P = 0.314), decreased heart rate (RR = 0.73, 95%CI: 0.51, 1.04; P = 0.080), decreased blood pressure (RR = 1.16, 95%CI: 0.81, 1.66; P = 0.417), and complication rate (RR = 0.62, 95%CI: 0.33, 1.15; P = 0.131).
Conclusion: The present study demonstrated that, propofol for sedation during colonoscopy can result in a faster recovery and discharge, a shorter time to sedation and ambulation, as well as improved patient satisfaction, but it did not increase the rate of complications. There is a need for more well-performed, large-scale trials to verify our findings.

1. Introduction

The use of sedation for routine endoscopic procedures varied greatly throughout the world [1]. Surgery data from USA suggest that > 98% of routine endoscopies are performed with sedation [2]. There are several kinds of sedative agents that have been used during the colonoscopy [3–5]. These agents could control patients' behavior and help them to complete the endoscopy procedure. However, not all the patients tolerate colonoscopy with sedation, and some even had discomfort experience. It is reported that about 20% of patients who underwent colonoscopy developed cardiorespiratory complications during the sedation [6]. The traditional sedative agent, such as benzodiazepines, has showed variable outcomes because of unstable levels of sedation [7]. This can result in patients discontent and difficulties in performing the endoscopy [7].

Propofol, used as an ultra-short-acting sedative agent, has gained increasing attention during the past few years [8]. It combines the major characteristics of an ideal sedative, such as a fast sedation onset, a short half-life, and a rapid recovery time [9]. Previous evidences have suggested that propofol has benefit effects even when it is administered by non-anesthesiologists, without leading to discomfort complications [10–12]. Moreover, several randomized controlled trials (RCTs) that

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evaluated the effects and safety of non-anesthesiologist administration propofol (NAAP) [13–15], have showed superior outcomes in safety and patient satisfaction. The aim of this study is to summary these trials and evaluate the effects, safety, and patient acceptance for colonoscopy as compared with traditional sedative agents.

2. Methods

2.1. Search strategy

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidelines [16]. Since this study did not involve the human or animal experiment, the ethical approval was not necessary.

We identified relevant literatures by searching PubMed, Embase, and Web of Science. The retrieval time was from their inception time to March 12, 2018. The search terms we used were as following: ("propofol"[MeSH Terms] OR "propofol"[All Fields]) AND sedation [All Fields] AND ("colonoscopy"[MeSH Terms] OR "colonoscopy"[All Fields]). We also performed a supplementary search of the reference lists from all included trials and reviews. Two investigators independently performed the title/abstract, full-text information review of the article that were potentially eligible for the inclusion criteria. For studies that did not provide available data, we contacted the corresponding author for the original data by email.

2.2. Inclusion criteria and exclusion criteria

Studies were included if they met the following criteria: (1) study design: RCT, or case-control study, or cohort study; (2) population: adult patients who were referred for colonoscopy; (3) intervention: propofol or propofol in combination with another sedative agents during colonoscopy; (4) comparison: traditional sedative agents for sedation during colonoscopy. (5) outcome measures: recovery time, procedure time, discharge time, pain score, satisfaction score, time to sedation/ambulation, and complication rate.

2.3. Data extraction

We used a prestandardised data extraction to extract data from the included studies. The following information were extracted: study design, country, author, year of publication, patients' characteristics (demographics and baseline characteristics), number of patients in each group, outcome measures (including recovery time, procedure time, discharge time, pain score, satisfaction score, time to sedation/ambulation, and complication rate). Any disagreement between the reviewers was resolved by discussion.

2.4. Quality assessment

The risk of bias in RCTs was evaluated using the method recommended by Cochrane Collaboration [17]. This method focuses on five domains, including blinding, method of randomization, allocation concealment, follow-up, and intention-to-treat analysis [17]. Each study was classified as high, low, or unclear risk of bias.

2.5. Statistical analysis

We use the STATA, version 12.0 (Stata Corporation, College Station, TX, USA) to perform all the statistical analyses. For dichotomous outcomes (such as complication rate), we calculated the risk ratio (RR) with 95% confidence interval (95%CI); for continuous outcomes (such as recovery time, procedure time, discharge time, pain score, and satisfaction score), we estimated weight mean difference (WMD) or standardized mean difference (SMD) with 95%CI. Before the data were pooled, we first tested the heterogeneity between the included studies, using I^2 statistic and Cochrane Q chi-square test [18]. $P < 0.10$ or $I^2 > 50\%$ were considered to be significant heterogeneity across the included studies [18]. A fixed-effects model [19] or random-effects model [20] was performed to pool the data according to the heterogeneity. When substantial heterogeneity was identified among the included studies, we conducted sensitivity analysis by omitting one study in turn to explore the potential sources of heterogeneity. Subgroup analysis was performed based on propofol alone VS in combination with another agents, anesthesiologist administration propofol (AAP) VS NAAP, and the type of comparators. The publication bias was assessed by Begg [21] and Egger's test [22]. A P value < 0.05 was judged as statistically significant, except where otherwise specified.

3. Results

3.1. Literature search

The initial search yielded 625 records from PubMed, Embase, and Web of Science. Of them, 483 were deleted because of duplicate records and 117 were excluded after the review of title/abstract, leaving 25 potential studies for full-text information review. However, among the remained studies, 6 were excluded because of the following reasons: four used propofol in both groups [23–26], one was a single-arm design [27], and one did not provide outcome of our interest [28]. Finally, nineteen studies [29–47] involving 2512 patients met the inclusion criteria and were included in this study (Fig. 1).

3.2. Characteristics of eligible studies

The main characteristics of included studies are presented in Table 1. All the included studies were prospective RCTs. These studies were published between 1998 and 2017. The sample size in each study ranged from 40 to 600, with a total number of 2512. The dosage of propofol varied greatly among the included studies, which ranged from 0.3 mg/kg to 1 mg/kg. Among the 19 studies, 7 studies [30–32, 34, 36, 40, 47] that evaluated AAP, and the remaining 12 studies [29, 33, 35, 37–39, 41–46] evaluated NAAP. The traditional sedative agents included midazolam, midazolam plus fentanyl, midazolam plus pethidine, remifentanil, midazolam plus meperidine, diazemuls plus pethidine/meperidine, diazolam plus nalbuphine.

The details of risk-of-bias assessment are summarized in Fig. 2. Overall, eight RCTs are classified as being at low risk of bias [30, 33, 38, 40, 42, 43, 46, 47], three at high risk of bias [32, 34, 36], and eight at unclear risk of bias [29, 31, 35, 37, 39, 41, 44, 45].

The reason for studies that had high risk of bias was that they did not perform the blinding of participants and personnel, or the blinding of outcome assessment. And the reason for studies that had unclear risk of bias was that the blinding was conducted, but the method was not detailedly reported.

3.3. Procedure time

Thirteen studies reported the data of procedure time [29, 30, 33–36, 39–41, 43–46]. The mean duration of procedure time in the propofol group and traditional sedative group were 18.97 min and 18.60 min, respectively. Pooled result showed that, patients in the propofol group had a comparable procedure time with those in traditional sedative group (WMD = −0.38 min, 95%CI: −0.84, 0.08; P = 0.108) (Fig. 3). The test for heterogeneity was not significant (I^2 = 8.2%, P = 0.364).

Subgroup analysis showed that propofol resulted in a similar procedure time with traditional sedative agents no matter it was administered alone (WMD = −0.37 min, 95%CI: −0.89, 0.14; P = 0.155) or in combination with another agents (WMD = −0.40 min, 95%CI: −1.44, 0.65; P = 0.454).

Subgroup analysis showed that AAP was associated with a shorter procedure time than other agents (WMD = −0.58 min, 95%CI: −1.07,