

# Anesthetic efficacy of propofol combined butorphanol in laparoscopic surgery for ectopic pregnancy

## A protocol of systematic review and meta-analysis

Wang-yan Chang, MB<sup>a</sup>, Hai-ying Li, MB<sup>b,\*</sup> 

### Abstract

**Background:** Recent studies have suggested that propofol combined butorphanol (PB) has anesthetic effect in laparoscopic surgery (LS) for ectopic pregnancy (EP). But investigations of its potential effects are inconsistent. We will explore the current literature examining PB in LS for EP.

**Methods:** We will perform a comprehensive search from MEDLINE, Embase, Cochrane Library, PsycINFO, Global Health, Web of Science, Allied and Complementary Medicine Database, and China National Knowledge Infrastructure from inception to the present. Other literatures, such as conference abstracts, references to the relevant reviews will also be checked. Two authors will check the titles, abstracts, and full texts independently. They will also independently carry out data collection and study quality assessment. We will conduct statistical analysis using RevMan 5.3 software.

**Results:** This study will provide accurate results on the anesthetic effect and safety of PB in LS for EP.

**Conclusion:** This study will establish high-quality evidence of the anesthetic effect and safety of PB in LS for EP to facilitate the clinical practice and guideline development.

**Study registration number:** INPLASY202040044.

**Abbreviations:** EP = ectopic pregnancy, LS = laparoscopic surgery, PB = propofol combined with butorphanol, RCTs = randomized controlled trials.

**Keywords:** anesthetic effect, butorphanol, ectopic pregnancy, laparoscopic surgery, propofol, safety

## 1. Introduction

Ectopic pregnancy (EP) is a known complication of pregnancy that often causes high maternal mortality and morbidity, and fetal loss.<sup>[1–3]</sup> Patients who experience such condition often manifest as pain, vaginal bleeding, or more vague complaints.<sup>[4–6]</sup> Published studies have reported that EP accounts for about 2% of pregnancies, and its incidence is about 1.5% to 2%.<sup>[7–10]</sup>

Thus, early diagnosis and effective treatment of EP is very important.<sup>[11,12]</sup>

Laparoscopic surgery (LS) is widely used for the treatment of EP.<sup>[13–16]</sup> During the process of LS, anesthetic medication is very important. Previous studies have found that propofol combined butorphanol (PB) can effectively manage EP patients under LS.<sup>[17–23]</sup> However, no systematic review has been identified to assess the anesthetic effect and safety of PB in LS for EP.

*This study was supported by Yan'an Specialized Project for Transformation and Promotion of Achievements (2018CGZH-15). The supporters had no role in this study.*

*The authors have no conflicts of interest to disclose.*

*Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.*

<sup>a</sup> Department of Gynecology and Obstetrics, <sup>b</sup> Department of Anesthesiology, Yan'an People's Hospital, Yan'an, China.

\* Correspondence: Hai-ying Li, Department of Anesthesiology, Yan'an People's Hospital, No 57 Qilipu Street, Baota District, Yan'an 716000, China (e-mail: haiyingli2007@aliyun.com).

Copyright © 2020 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Chang Wy, Li Hy. Anesthetic efficacy of propofol combined butorphanol in laparoscopic surgery for ectopic pregnancy: a protocol of systematic review and meta-analysis. *Medicine* 2020;99:20(e20289).

Received: 14 April 2020 / Accepted: 16 April 2020

<http://dx.doi.org/10.1097/MD.00000000000020289>

## 2. Methods

### 2.1. Study registration

This study has been registered prospectively on INPLASY202040044. We report this study according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol 2015 statement.<sup>[24]</sup>

### 2.2. Criteria for including studies

**2.2.1. Types of studies.** We will review randomized controlled trials (RCTs) of anesthetic effect and safety of PB in LS for EP for inclusion. Animal studies, descriptive studies, case studies, noncontrolled trials, and quasi-RCTs will be excluded in this study.

**2.2.2. Types of interventions.** In the experimental group, all patients received PB intervention.

In the control group, all participants underwent any interventions, except PB.

**2.2.3. Types of patients.** All female participants who were diagnosed as EP under LS and received PB will be included in this study with no restrictions of country, race, and age.

**2.2.4. Types of outcome measurements.** The primary outcome includes pain intensity, as measured by any pain scales, such as numerical rating scales.

The secondary outcomes consist of analgesic consumption; concurrent medication; laboratory parameters; quality of life, as checked by any relevant tools, such as 36-Item Short Form Survey; and any adverse events.

### 2.3. Search strategy

We will comprehensively search following databases from inception to the present: MEDLINE, Embase, Cochrane Library, PsycINFO, Global Health, Web of Science, Allied and Complementary Medicine Database, and China National Knowledge Infrastructure from inception to the present. All electronic databases will be searched without limitations of language and publication status. The search terms include ectopic pregnancy, extrauterine pregnancy, surgery, operation, laparoscopic surgery, pain intensity, anesthetic effect, propofol, anesthesia S/I-60, anesthesia S/I-40, anesthesia S/I-40A, butorphanol, and stadol. We will list a search strategy for MEDLINE in Table 1. Similar search strategies will be modified for other different databases.

To avoid missing any potential studies, we will search grey literatures, such as conference abstracts, and references of relevant reviews.

### 2.4. Data collection and analysis

**2.4.1. Study selection.** Two authors will screen the titles and abstracts of all identified records independently and respectively. All irrelevant records will be removed. Then, we will obtain full texts of all remaining studies fulfilling the eligible criteria, and will check all of them for inclusion. Any different opinions in the checking process will be adjudicated by a 3rd author. We will present the whole process of study selection in a flowchart, and any excluded studies will be recorded with specific reasons.

**2.4.2. Data extraction.** Two authors will independently extract data based on the standard previously defined data extraction sheet to ensure the integrity of the process. Any different views between 2 authors will be solved by a 3rd author through discussion. The following information will be extracted: study title, 1st author, year of publication, country, inclusion and exclusion criteria, diagnostic criteria, race, age, sample size, study setting, study methods, treatment details, outcome measurements, safety, and any other relevant information. If any data are missing or unclear, we will contact original authors to obtain or clarify it.

**2.4.3. Risk of bias assessment.** We will evaluate the risk of bias from the entered studies using Cochrane risk of bias tool for RCTs, and all 7 relevant fields of bias will be checked. Each one will be further identified as low, unclear or high risk of bias. Two authors will independently assess the risk of bias, and any discrepancies between 2 authors will be examined by a 3rd author through discussion to make a decision.

### 2.5. Data synthesis

We will apply RevMan 5.3 software to perform statistical analysis. All dichotomous data will be calculated using risk ratio

**Table 1**

**Search strategy of MEDLINE.**

Number	Search terms
1	Ectopic pregnancy
2	Extrauterine pregnancy
3	Tubal pregnancy
4	Fertilized egg
5	Pelvic pain
6	Vaginal bleeding
7	Or 1–6
8	Laparoscopic surgery
9	Surgery
10	Operation
11	Laparoscopy
12	Surgical technique
13	Or 8–12
14	Anesthetic effect
15	Pain intensity
16	Propofol
17	Anesthesia S/I-60
18	Anesthesia S/I-40
19	Anesthesia S/I-40A
20	Butorphanol
21	Stadol
22	Or 14–21
23	Randomized controlled trials
24	Clinical trials
25	Random
26	Randomly
27	Control
28	Allocation
29	Placebo
30	Blind
31	Trials
32	Clinical study
33	Or 23–32
34	7 and 13 and 22 and 33

and 95% confidence intervals, while all continuous data will be expressed using mean difference or standardized mean difference and 95% confidence intervals. We will  $I^2$  statistics to identify potential heterogeneity among included studies and will be explained as follows:  $I^2 \leq 50\%$  means low heterogeneity, and a fixed-effects model will be imposed; while  $I^2 > 50\%$  exerts obvious heterogeneity, and a random-effects model will be used. If low heterogeneity will be found among the eligible studies, we will perform meta-analysis on the same interventions, controls, and outcomes. If obvious heterogeneity will be identified, we will carry out subgroup analysis to check if there are some possible reasons for obvious heterogeneity. In addition, if it is possible, we will undertake a narrative description of the outcome results using detailed written commentary base on the different target patients, treatment details, controls, and outcome measurements.

**2.5.1. Subgroup analysis.** Subgroup analysis will be undertaken based on the different study and patient characteristics, study quality, treatments, controls, and outcomes.

**2.5.2. Sensitivity analysis.** Sensitivity analysis will be carried out to check the stability of outcome results by removing low-quality studies.

**2.5.3. Reporting bias.** Reporting bias will be identified through funnel plot and Egger regression test when sufficient studies are entered in this study, normally at least 10 RCTs.<sup>[25,26]</sup>

### 3. Discussion

Numerous studies have reported the anesthetic effect and safety of PB in LS for EP.<sup>[17–23]</sup> However, there are still contrary results of these studies, and there is not systematic review reporting the anesthetic effect and safety of PB in LS for EP. Therefore, this study will systematically and comprehensively investigate the anesthetic effect and safety of PB in LS for EP. The findings of this study will present beneficial evidence for the clinical practice and will provide helpful clue for the future research.

#### 3.1. Ethics and dissemination

Ethical documents are not required for this study, because it will not inquire personal patient data. We will publish this study in a peer-reviewed journal.

#### Author contributions

**Conceptualization:** Wang-yan Chang, Hai-ying Li.

**Data curation:** Wang-yan Chang, Hai-ying Li.

**Formal analysis:** Wang-yan Chang, Hai-ying Li.

**Funding acquisition:** Hai-ying Li.

**Investigation:** Hai-ying Li.

**Methodology:** Wang-yan Chang.

**Project administration:** Hai-ying Li.

**Resources:** Wang-yan Chang.

**Software:** Wang-yan Chang.

**Supervision:** Hai-ying Li.

**Validation:** Wang-yan Chang, Hai-ying Li.

**Visualization:** Wang-yan Chang, Hai-ying Li.

**Writing – original draft:** Wang-yan Chang, Hai-ying Li.

**Writing – review & editing:** Wang-yan Chang, Hai-ying Li.

#### References

- [1] Glenn TL, Bembry J, Findley AD, et al. Cesarean scar ectopic pregnancy: current management strategies. *Obstet Gynecol Surv* 2018;73:293–302.
- [2] Abubakar P, Nwobodo E, Omokanyo O, et al. Ectopic pregnancy at Usmanu Danfodiyo University teaching hospital Sokoto: a ten-year review. *Ann Niger Med J* 2012;6:87–91.
- [3] Brady PC. New evidence to guide ectopic pregnancy diagnosis and management. *Obstet Gynecol Surv* 2017;72:618–25.
- [4] Zahálková L, Kacerovský M. Cesarean scar ectopic pregnancy [in Czech]. *Ceska Gynekol Winter* 2016;81:414–9.
- [5] Parker VL, Srinivas M. Non-tubal ectopic pregnancy. *Arch Gynecol Obstet* 2016;294:19–27.
- [6] Taran FA, Kagan KO, Hübner M, et al. The diagnosis and treatment of ectopic pregnancy. *Dtsch Arztebl Int* 2015;112:693–703.
- [7] Farquhar CM. Ectopic pregnancy. *Lancet* 2005;366:583–91.
- [8] Committee on Practice, Bulletins—Gynecology/ACOG Practice Bulletin No. 191: Tubal Ectopic Pregnancy. *Obstet Gynecol* 2018;131:e65–77.
- [9] Mikhail E, Salemi JL, Schickler R, et al. National rates, trends and determinants of inpatient surgical management of tubal ectopic pregnancy in the United States, 1998–2011. *J Obstet Gynaecol Res* 2018;44:730–8.
- [10] van Mello NM, Zietse CS, Mol F, et al. Severe maternal morbidity in ectopic pregnancy is not associated with maternal factors but may be associated with quality of care. *Fertil Steril* 2012;97:623–9.
- [11] Mooij R, Geomini P, Bongers MY. Ectopic pregnancy. *Ned Tijdschr Geneesk* 2014;158:A7831.
- [12] Belics Z, Gérecz B, Csákány MG. Early diagnosis of ectopic pregnancy [in Hungarian]. *Orv Hetil* 2014;155:1158–66.
- [13] Sowter MC, Farquhar CM, Gudex G. An economic evaluation of single dose systemic methotrexate and laparoscopic surgery for the treatment of unruptured ectopic pregnancy. *BJOG* 2001;108:204–12.
- [14] Lundorff P. Laparoscopic surgery in ectopic pregnancy. *Acta Obstet Gynecol Scand Suppl* 1997;164:81–4.
- [15] Dubuisson JB, Chapron C, Morice P, et al. Radical laparoscopic surgery of ectopic pregnancy: results from a continuous series of 383 interventions. *Contracept Fertil Sex* 1996;24:140–6.
- [16] Lundorff P, Thorburn J, Hahlin M, et al. Laparoscopic surgery in ectopic pregnancy. A randomized trial versus laparotomy. *Acta Obstet Gynecol Scand* 1991;70:343–8.
- [17] Chen KD, Wang XG, Zhuo R. Comparison of anesthesia effect of etomidate and propofol induced by general anesthesia during laparoscopic surgery in ectopic pregnancy. *China Contemp Med* 2019;26:162–4.
- [18] Zhang YN. Discussion on the effect of remifentanyl combined with propofol anesthesia in ectopic pregnancy. *Chin Med Guide* 2017;15:71–2.
- [19] Lin J, Li LZ, Wang XF. The clinical effect of target-controlled infusion of remifentanyl combined with propofol for gynecological laparoscopic anesthesia. *Primary Med Forum* 2016;20:1350–1.
- [20] Lai YM. Clinical application of propofol combined with ketamine anesthesia in laparoscopic surgery for ectopic pregnancy. *Jilin Med* 2013;34:2958.
- [21] Shi H. Application effect analysis of propofol combined with ketamine anesthesia in laparoscopic surgery for ectopic pregnancy. *Chin J Pract Med* 2012;7:134–5.
- [22] Zhang Y, Hu YM, Guo LF, et al. Observation of anesthesia effect of different concentrations of target-controlled infusion of propofol and remifentanyl during laparoscopic ectopic pregnancy. *China Coal Industry Med J* 2009;12:191–3.
- [23] Li HF, Yang P, Lin YG, et al. Analysis of 68 cases of combined anesthesia with propofol and ketamine for laparoscopic surgery of ectopic pregnancy. *J Pract Obstet Gynecol* 2005;9:567–9.
- [24] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349:g7647.
- [25] Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. *J Clin Epidemiol* 2005;58:882–93.
- [26] Guyatt GH, Oxman AD, Kunz R, et al. Incorporating considerations of resources use into grading recommendations. *BMJ* 2008;336:1170–3.