



Efficacy and safety of epidural anesthesia versus local anesthesia in percutaneous transforaminal endoscopic discectomy: a systematic review and meta-analysis

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Background: For some patients, local anesthesia (LA) in percutaneous transforaminal endoscopic discectomy (PTED), especially during canal shaping and discectomy, is insufficient for analgesia. Epidural anesthesia (EA) is infrequently applied in PTED but reports satisfactory results. Previous studies present conflicting results in analgesia satisfactory and adverse events. Differences in surgery details and small sample size might explain conflicting results. Meta-analysis pools the results from individual studies to create a larger sample size and provides a more reliable conclusion. The aim of this study is to evaluate the efficacy and safety of EA in PTED.

Methods: The search terms “percutaneous transforaminal endoscopic discectomy” and “anesthesia” are used to search Cochrane, Web of Science, PubMed, Embase, OVID, China National Knowledge Infrastructure (CNKI), VIP, and Wanfang from inception to 2021-08. Inclusion criteria is defined according to PICOS principals: P (patients): patients are diagnosed with lumbar disc herniation or spinal canal stenosis. I (intervention): patients undergo PTED under EA. C (comparisons): patients undergo PTED under LA. O (outcomes): primary outcomes: intraoperative visual analogue scale (VAS), anesthesia satisfactory, sufentanil usage. Secondary outcomes: adverse events, surgery exit, bleed volume, X-ray radiation. S (study design): randomized controlled trials (RCTs). The Cochrane RoB 2.0 is used to evaluate the quality of the included studies. Authors perform meta-analysis through Review Manager 5.4.

Results: A total of 6 studies representing 529 patients are included: EA group includes 261 patients, and LA group includes 268 patients. All studies lack design of allocation concealment and blinding of participants and personnel. Only Luo reports blinding of outcome assessment in 2019. Meta analysis concludes that EA is superior in intraoperative analgesic [mean difference (MD) = -4.31; 95% confidence interval (CI): -4.52 to -4.09; P < 0.00001], anesthesia satisfactory [odds ratio (OR) = 10.06; 95% CI: 2.41 to 41.98; P = 0.002], sufentanil usage (MD = -9.12; 95% CI: -10.34 to -7.90; P < 0.00001), adverse events (OR = 0.19; 95% CI: 0.07 to 0.52; P = 0.001). There is no difference in bleed volume (MD = -2.61; 95% CI: -5.45 to 0.23; P = 0.07), exit rate (OR = 0.23; 95% CI: 0.04 to 1.35; P = 0.10) and future effects (MD = -0.23; 95% CI: -0.50 to 0.03; P = 0.08).

Discussion: EA is an effective and safe anesthesia method for PTED and might achieve better clinical results than LA. More high-quality research is needed to provide high-quality evidence for efficacy and safety.

Keywords: Percutaneous transforaminal endoscopic discectomy (PTED); local anesthesia (LA); epidural anesthesia (EA); meta-analysis

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Introduction

Due to occupational factors and aging population, the occurrence of spine disorders such as lumbar disc herniation and spinal canal stenosis is surging (1,2). When conservative management fails, appropriate surgical treatment is the last choice for patients (3). With the advantage of minimally invasive, enhanced recovery and satisfactory effects, percutaneous transforaminal endoscopic discectomy (PTED) has been used as safe and effective therapy for spine diseases (4).

Anesthesia is an essential part of successful surgery. Surgeons can perform PTED under different anesthesia methods and the most frequently used method is local anesthesia (LA). Under LA, patients are awake during the whole surgery procedure, and surgeons can communicate with patients to get instant feedback to avoid nerve damage especially sciatic nerve and femoral nerve. However, for some patients, inadequate anesthesia effects, unsatisfactory surgery experience, and more needs for opioids question LA's analgesic efficacy (5,6). PTED under general anesthesia can achieve adequate analgesia during the whole surgery procedure. However, due to the lack of communication, surgeons have to avoid damaging nerve carefully, especially during canal shaping and discectomy (7).

Epidural anesthesia (EA) is also a mature anesthesia method in surgery. Anesthetist injects anesthetic drugs into epidural space, and spinal nerve roots penetrating this space will be blocked to achieve anesthesia effects. According to pain conduction pathway, dorsal spine nerves transmit pain sensory signals from peripheral nerves to the spine (8). In theory, under EA, pain control is superior to LA. However, the EA technique is more complex than LA, and unique adverse events cannot be neglected. PTED under EA can achieve both communications between surgeons and patients to avoid nerve damage and better pain control. Therefore, it can be considered as a potentially feasible anesthesia method for PTED (9,10).

Previous study (11) have reported EA in PTED. However, the inclusion criteria is not rigorous and it neglects several studies and some valuable outcomes. Sun includes retrospective studies rather than exclusive randomized controlled trials (RCTs) for meta-analysis, and

2 randomized clinical trials (12,13) are not included in the review. Outcomes including opioids usage and surgery exit are not analyzed. Besides analgesic effects, randomized clinical trials have presented conflicting outcomes in adverse events, anesthesia satisfactory. Luo *et al.* (14) reports similarity in 2019, but in 2017 Wang *et al.* (15) reports superiority of EA in complications. Zhang *et al.* (12) reports similarity in 2019, but Luo reports similarity in anesthesia satisfactory. The conflicting results can be contributed to: (I) different dose of analgesic drugs, different anesthetists and different surgeons. (II) The statistical power may be limited due to small sample. Meta-analysis, a statistical tool currently used for large-scale data analysis, pools the results from individual studies to create a larger sample size and provides more reliable conclusion. In order to evaluate the efficacy and safety of EA in PTED, we perform this study to review published studies and perform pooled-analysis to compare EA and LA in PTED surgery. We present the following article in accordance with the PRISMA reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-21-3413/rc>).

Methods

Search strategy

In order to collect comprehensive published studies, we use “percutaneous transforaminal endoscopic discectomy” and “anesthesia” in Cochrane, PubMed, OVID, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), Wanfang Database, and VIP Database from inception to 2021-08, to review relevant studies. Potentially related studies are manually searched by authors.

Inclusion criteria

- ❖ P (patients): patients are diagnosed with lumbar disc herniation or spinal canal stenosis. Patients diagnosed with deformity, infection, tuberculosis, tumor will be excluded.
- ❖ I (intervention): patients who undergo PTED under EA.

- ❖ C (comparisons): patients who undergo PTED under LA. If the study is three-arm design, we will apply analysis between LA and EA.
- ❖ O (outcomes): the primary outcomes are efficacy relevant: intraoperative visual analogue scale (VAS), anesthesia satisfactory, sufentanil usage. The secondary outcomes are safety relevant: adverse events, surgery exit, bleed volume, X-ray radiation. Eligible studies should include at least one item of primary or secondary outcomes.
- ❖ S (study design): all included studies are RCTs. Retrospective studies and case reports are excluded due to low evidence level.

Studies selection

Two authors independently read titles as first selection and then read abstracts as second selection. Then authors read full texts as the third selection process and then evaluate the risk of bias of included studies. Discrepancy is solved by correspondence author (HL) during the whole procession.

Risk of bias

Two authors evaluate risks of included studies according to Cochrane Rob 2.0 outlined by the Cochrane Collaboration independently. Seven items are evaluated: (I) random sequence generation; (II) allocation concealment; (III) blinding of participants and personnel; (IV) blinding of outcome assessment; (V) incomplete outcome data; (VI) selective reporting; (VII) other bias. If authors do not report relevant design details, we regard this item as high bias.

Data extraction

(I) Study information: the study is renamed as the combination of last name of first author and publication year. (II) Sample size. (III) Primary outcomes: intraoperative VAS, anesthesia satisfactory, sufentanil usage. (IV) Secondary outcomes: adverse events, surgery exit, bleed volume, X-ray radiation. We compare the highest VAS between EA and LA to evaluate the analgesic effects. YH correct extracted data.

Statistical analysis

We perform meta-analysis through Review Manager 5.4 in qualified studies. For continuous variables, we report mean

differences (MDs) with 95% confidence intervals (CIs). For categorical variables, we calculate odds ratios (ORs) and 95% CIs. We apply Chi-squared and I^2 tests to assess statistical heterogeneity. If $I^2 > 50\%$, the results are regarded with high heterogeneity, and random-effects model is used; otherwise, we perform fixed-effects model to analyze data. Sensitivity analyses assess the susceptibility of the findings of this meta-analysis. The funnel plot will be used to evaluate the existence of publication bias if the number of included studies is more than 10. Once potential reporting bias is detected, Beggs and Eggers test are used to evaluate the symmetry of the funnel plot and publication bias. P values less than 0.05 is considered statistically significant.

Results

Summarize of studies

A total of 923 studies are extracted from 8 databases. After selection, finally 6 studies (9,12-16) fulfill inclusion criteria. The selection process details are seen in *Figure 1*. Six studies (9,12-16) representing 529 patients are included in our meta-analysis. EA group includes 261 patients, and LA group includes 268 patients. The characteristic details are shown in *Table 1*.

Risk of bias

Six studies (9,12-16) apply randomization in their design. All studies lack design of allocation concealment and blinding of participants and personnel. Only Luo reports blinding of outcome assessment to avoid measurement bias. The details of bias are shown in *Figure 2*.

Results of summarized data

Intraoperative VAS

Three studies report (9,14,16) improved intraoperative VAS in their design. And pooled-analysis indicates better analgesic in EA group (MD = -4.31, 95% CI: -4.52 to -4.09, $P < 0.00001$; heterogeneity $\text{Chi}^2 = 0.26$, $\text{df} = 2$, $P = 0.88$, $I^2 = 0\%$). The result is shown in *Figure 3*.

Anesthesia satisfactory

Two studies (12,14) report anesthesia satisfactory. Luo *et al.* indicates that patient experience better anesthesia satisfactory and Zhang *et al.* (12) shows no difference. Pooled-analysis shows that anesthesia satisfactory is better in EA (OR

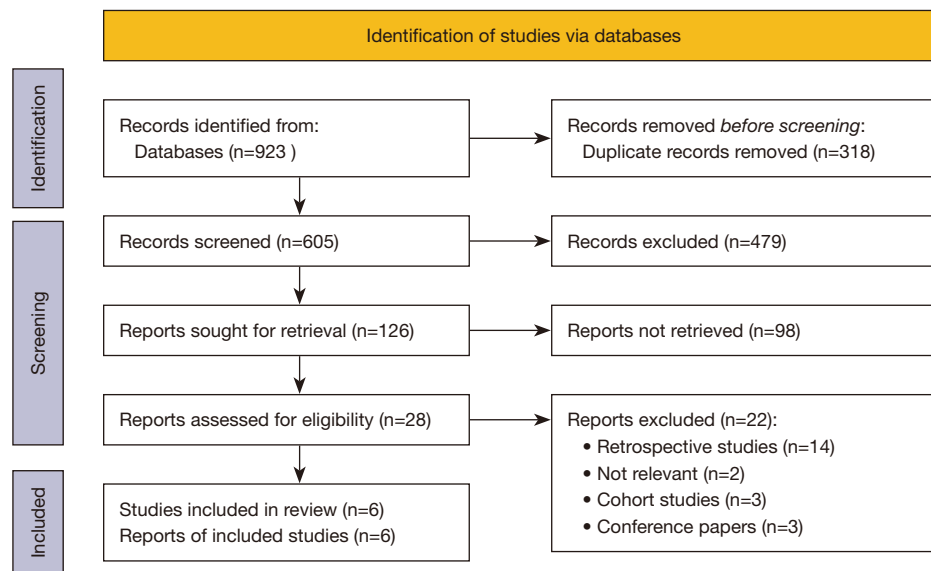


Figure 1 A flow diagram of literature search and study selection.

Table 1 Studies characteristic

Author, year	Participants (EA/LA)	Age (EA/LA), years, mean \pm SD	Anesthesia method (EA/LA)
Huang, 2014	20/20	35 \pm 17/36 \pm 15	10 μ g sufentanil and 40 mg ropivacaine/2% lidocaine
Wang, 2017	46/46	43.56 \pm 4.42/44.82 \pm 3.53	0.12% ropivacaine and sufentanil/1% lidocaine
Luo, 2019	25/25	35 \pm 15/33 \pm 17	3 mL 2% lidocaine for test and 15 mL 0.3% ropivacaine/0.5% lidocaine 20 mL
Xu, 2019	49/49	42.52 \pm 15.307/44.88 \pm 13.535	0.3% ropivacaine/mixture of 0.2% ropivacaine and 0.4% lidocaine
Zhang, 2019	20/25	48 \pm 10/46 \pm 8	3 mL of 1% lidocaine and 0.2% ropivacaine 7 mL/0.5% lidocaine 20 mL
Zhang, 2020	101/103	40.01 \pm 11.18/39.68 \pm 11.56	3 mL of 2% lidocaine for test and 10 mL of 0.125% ropivacaine with 0.2 μ g/mL sufentanil/1% lidocaine 13 mL

EA, epidural anesthesia; LA, local anesthesia.

=10.06, 95% CI: 2.41 to 41.98, $P=0.002$; heterogeneity $\text{Chi}^2=0.26$, $df=1$, $P=0.61$, $I^2=0\%$), shown in *Figure 4*.

Sufentanil use

Three studies (12-14) report less application of sufentanil use in EA group, and 2 studies (12,13) group report usage details. The pooled analysis of 2 studies shows that EA is superior in reducing sufentanil usage (MD = -9.12 , 95% CI: -10.34 to -7.90 , $P<0.00001$; heterogeneity $\text{Chi}^2=0.73$, $df=1$, $P=0.39$, $I^2=0\%$), shown in *Figure 5*.

Surgery exit

Two studies (9,16) report 7 of total 302 patients quit during surgery. We record their reasons for withdrawal: in EA group, 1 patient quits due to failure of catheterization. In LA group, 2 patients quit before surgery due to fear and 4 patients quit during surgery due to pain or hemodynamic fluctuations. There is no difference between LA and EA in exit rate (OR = 0.23 , 95% CI: 0.04 to 1.35, $P=0.10$; heterogeneity $\text{Chi}^2=0.23$, $df=1$, $P=0.63$, $I^2=0\%$), shown in *Figure 6*.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Huang 2014	+	-	-	-	+	+	+
Luo 2019	+	-	-	+	+	+	+
Wang 2017	+	-	-	-	+	+	+
Xu 2019	+	-	-	-	+	+	+
Zhang 2019	+	-	-	-	+	+	+
Zhang 2020	+	-	-	-	+	+	+

Figure 2 Summary of risk bias of included studies. Green shading indicates low risk of deviation. Red indicates high risk of deviation.

Adverse events

Two studies (14,15) report 28 adverse events in perioperative phase. In EA group, 6 of 71 patients are reported with adverse events and 22 of 71 patients are reported. Wang *et al.* report EA is superior, but Luo *et al.* indicates there is no difference. The pooled-effects reports that patient will suffer less adverse events under EA (OR =0.19, 95% CI: 0.07 to 0.52, P=0.001; heterogeneity $\chi^2 =0.00$, df =1, P=0.97, $I^2=0\%$), shown in *Figure 7*.

Blood volume

Three studies (9,12,13) report blood volume during surgery, and pooled analysis indicates there is no difference between EA and LA group (MD =-2.61, 95% CI: -5.45 to 0.23, P=0.07; heterogeneity $\chi^2 =1.37$, df =2, P=0.50, $I^2=0\%$), *Figure 8*.

Future effects

Three studies (9,14,16) report future effects concentrating on pain evaluation. Xu *et al.* reports EA is better, but Luo and Zhang *et al.* (9) report no difference. The pooled-analysis concludes there is no difference between EA and LA (MD =-0.23, 95% CI: -0.50 to 0.03, P=0.08; heterogeneity $\chi^2 =4.28$, df =2, P=0.12, $I^2=53\%$), shown in *Figure 9*.

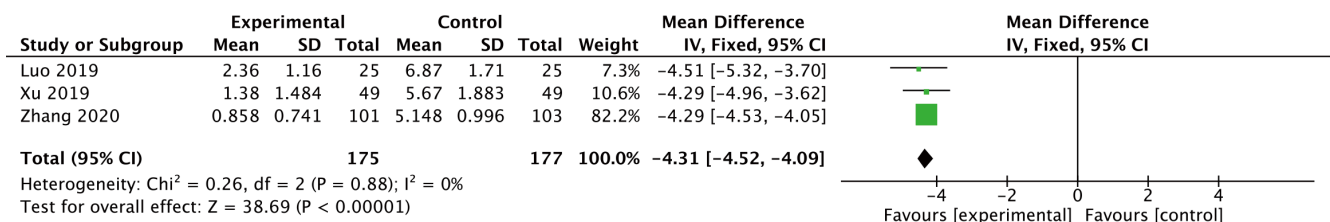


Figure 3 Forest plot of intraoperative VAS score between EA and LA. Experimental group = EA group. Control group = LA group. CI, confidence interval; VAS, visual analogue scale; EA, epidural anesthesia; LA, local anesthesia.

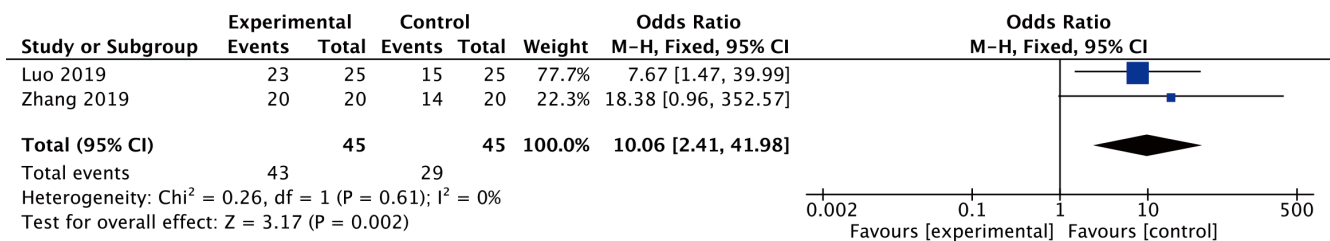


Figure 4 Forest plot of anesthesia satisfactory between EA and LA. Experimental group = EA group. Control group = LA group. CI, confidence interval; EA, epidural anesthesia; LA, local anesthesia.

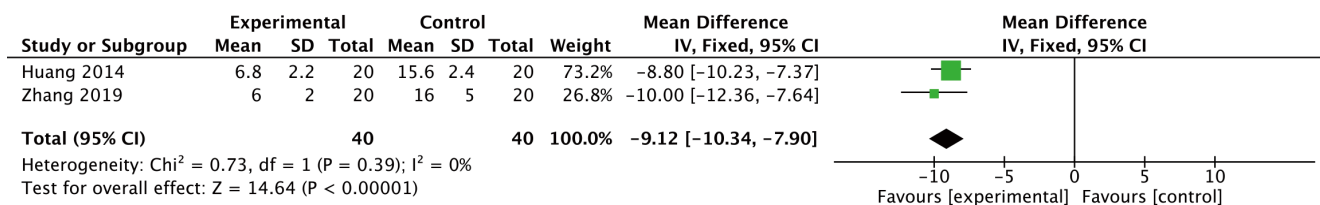


Figure 5 Forest plot of sufentanil use between EA and LA. Experimental group = EA group. Control group = LA group. CI, confidence interval; EA, epidural anesthesia; LA, local anesthesia.

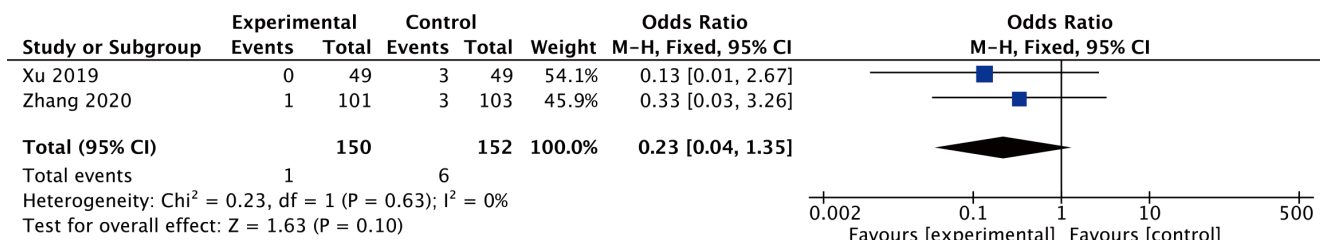


Figure 6 Forest plot of surgery exit between EA and LA. Experimental group = EA group. Control group = LA group. CI, confidence interval; EA, epidural anesthesia; LA, local anesthesia.

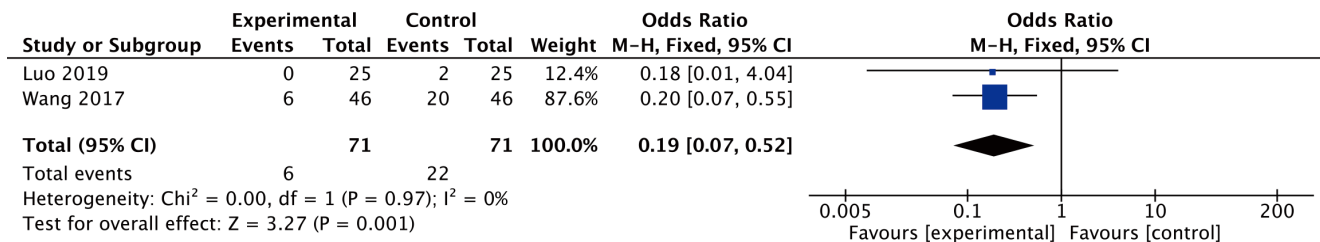


Figure 7 Forest plot of adverse events between EA and LA. Experimental group = EA group. Control group = LA group. CI, confidence interval; EA, epidural anesthesia; LA, local anesthesia.

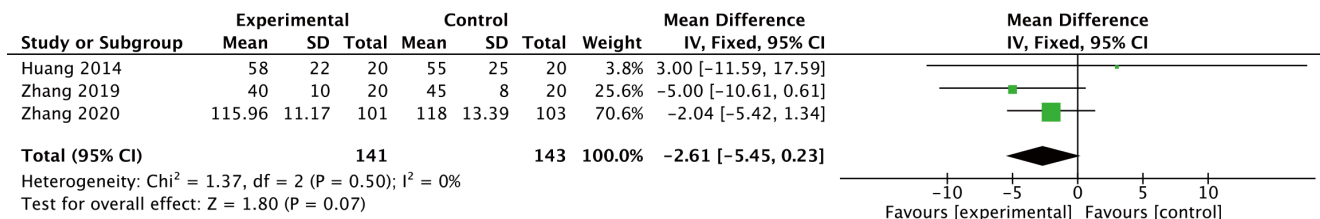


Figure 8 Forest plot of blood volume between EA and LA. Experimental group = EA group. Control group = LA group. CI, confidence interval; EA, epidural anesthesia; LA, local anesthesia.

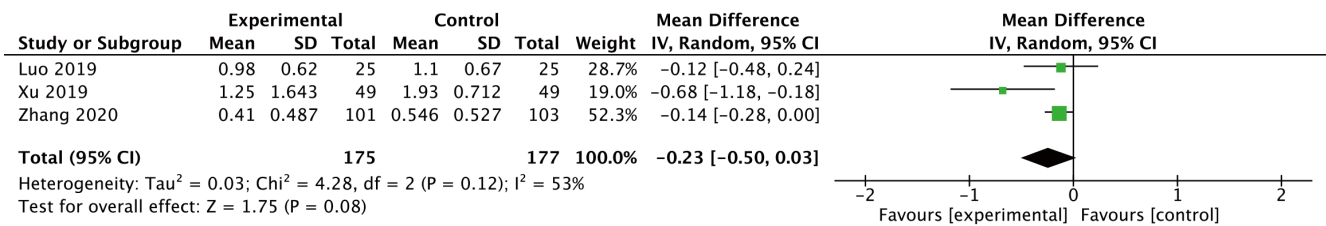


Figure 9 Forest plot of future effects between EA and LA. Experimental group = EA group. Control group = LA group. CI, confidence interval; EA, epidural anesthesia; LA, local anesthesia.

Publication bias

Due to the limited number of studies, we can not perform funnel plot analysis to detect publication bias.

Discussion

In spine surgery, PTED have consistent theoretical basis with open surgery: relieve compression, improve tissue inflammation and reconstruct spinal stability. Compared with traditional open surgery, PTED leads to reduced trauma and lower incidence of severe complications in patients (17,18).

Satisfactory analgesia is an essential part of successful operation. The current mainstream anesthesia methods include general anesthesia, intravertebral anesthesia and LA. As for anesthesia selection, surgeons should consider the patients conditions, disease progression and the operation procedure. LA blocks the nerve endings of local tissues to block the pain transmission. EA injects local anesthetics into the epidural space and blocks the pain conduction in spinal nerves. At the same time, EA can also extend the duration of anesthesia and adjust the plane of anesthesia through epidural catheter placement. It is used more in cesarean section and gynecological anesthesia (19).

In order to avoid nerve damage, surgeons perform PTED under LA. But the efficacy of LA is not always adequate. During surgery, pulling of spinal nerves is inevitable. Some patients change the anesthesia method during surgery or even withdraw because they cannot tolerate severe pain. Related literatures report that pain mainly concentrates in puncture needle, foraminoplasty, and discectomy. Therefore, effective anesthesia method is part of safe and successful PTED. EA is infrequently applied in PTED, but previous studies have reported better analgesic effects of EA in PTED. The purpose of this study is to evaluate the efficacy and safety of EA in PTED.

Our research suggests that analgesic effect of EA in intraoperative pain is better than LA. All included studies report better analgesic effects of EA and pooled-analysis reveals low heterogeneity between included studies. Peripheral pain is conducted to the spinal cord through spinal nerves. EA blocks spinal nerve than peripheral nerve to achieve analgesia. Meta-analysis result is in line with theoretical result and previous study results. The included studies report several VAS outcomes during surgery, and Included studies apply different pain evaluation methods: (I) specific time point; (II) specific surgical procedure point. This research focuses on the comparison of patients' maximum pain during surgery. The pain intensity is the major factors influencing surgery exit, anesthesia satisfactory, and opioids usage. In our stereotype, patients are prone to quit surgery during canal shaping and discectomy because they can not tolerate severe pain. But in our analysis, two studies report no difference between LA and EA in surgery exit and meta-analysis indicates no difference between EA and LA. Although sometimes LA is not adequate enough for PTED anesthesia, it is still an effective and safe anesthesia method for PTED. But due to better pain control, EA is superior to LA in anesthesia satisfactory.

There is no significant difference in bleeding volume between LA and EA. In the study of Xu *et al.*, it is reported that EA could also reduce the cumulative amount of radiation during surgery and reduce cumulative radiation for surgeons (16).

As for postoperative complications, EA is also superior to LA. On the one hand, due to inadequate analgesic effects, LA leads to sympathetic overaction and inflammatory reactions with potentially harmful effects in postoperative complications and longer hospital stays. Wang's study reports the immune function of LA after surgery is more active. On the other hand, more opioids will be needed to offset analgesia deficiency. As a typical opioid analgesic,

sufentanil provides satisfactory pain control effect. But its side effects such as postoperative respiratory depression, nausea and vomiting may also be the cause of postoperative complications. There are 3 literature reports that sufentanil usage for analgesia during surgery. In comparison of sufentanil usage, EA is superior to LA. The above result indicate that EA is superior to LA in pain control, therefore, less extra sufentanil is needed to offset analgesia deficiency. In recent years, opioid-related adverse events and abuse have promoted the development of opioid-free anesthesia. For spine-related diseases, patients may take painkillers, including opioids for long time before surgery. Therefore, in PTED anesthesia, reducing the use of opioids may reduce postoperative complications and lead to better life quality after surgery.

In terms of long-term effects, there is no significant difference between LA and EA. LA and EA are only different anesthesia methods. The purpose of PTED is to relieve oppression of nerve roots or spinal cord by eliminating hyperplastic bone or herniated intervertebral discs. Whether PTED under EA or LA, adequate nerve decompression is the key factor to future outcomes.

Limitations

The deficiencies of this study are as follows: (I) the included studies are all reported by Chinese researchers, and there is a lack of reports from other countries and regions. (II) In the quality evaluation, all studies lack allocation concealment and blinding of participants and personnel. At the same time, only one study applies blinding of outcome assessment in the design, which may introduce selection bias and information bias. (III) The recordings of pain evaluation in studies are different. There are 2 methods: (I) specific time point; (II) specific surgical procedure point. Pain evaluation according to specific surgical procedure is preferred. Time point varies according to surgeons' experience and pathology area, however, the worst pain mainly focuses on canal shaping and discectomy. Therefore, pain evaluation according to specific surgical procedure point is more reasonable.

Conclusions

EA is an effective and safe anesthesia method for PTED and might achieve better clinical results than LA. More high-quality research is needed to provide high-quality evidence for efficacy and safety.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at <https://apm.amegroups.com/article/view/10.21037/apm-21-3413/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroups.com/article/view/10.21037/apm-21-3413/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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