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The effect of preoperative administration of morphine in alleviating intraoperative pain of percutaneous transforaminal endoscopic discectomy under local anesthesia

A STROBE compliant study

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Abstract

Local anesthesia is routinely recommended for percutaneous transforaminal endoscopic discectomy (PTED). However, the intense intraoperative pain remains a serious problem. The purpose of the current study is to find a safe and effective method to alleviate the intense pain during PTED for lumbar disc herniation (LDH) under local anesthesia.

This study retrospectively analyzed 63 LDH patients who accepted PTED under local anesthesia. Thirty-one patients received intramuscular injection of morphine before PTED, while the other 32 were not. The 10 points visual analogue scale (VAS) was used to assess the patients' maximum leg and back pain. Patients were asked to grade their experiences of surgery and anesthesia on a 5-point Likert-type scale after the surgery. Modified Mac Nab Criteria were used to evaluate the surgical outcomes after 3-month follow-up.

The intraoperative VAS scores of patients who accepted preoperative intervention decreased significantly. The postoperative VAS scores of both groups showed no significance. Patients who received preoperative intervention reported a higher subjective satisfaction rate with the surgery experience. According to the Modified Mac Nab criteria, the surgical outcomes of both groups were similar through the 3-month follow-up. After injection of morphine, 4 patients complained nausea and 2 patients experienced vomiting.

Preoperative intramuscular injection of morphine could reduce the patients' pain during the PTED surgery and improve the patients' satisfaction without affecting the surgical outcome. Except for a higher incidence of nausea and vomiting, this method is relatively safe and convenient.

Abbreviations: 95% CI = 95% confidence interval, ES = effect size, GABA$_A$ = γ-aminobutyric acid subtype A, LDH = lumbar disc herniation, PTED = percutaneous transforaminal endoscopic discectomy, SP = statistical power, VAS = visual analogue scale.

Keywords: local anesthesia, lumbar disc herniation, morphine, percutaneous transforaminal endoscopic discectomy

1. Introduction

Percutaneous transforaminal endoscopic discectomy (PTED) is one of the most widely used minimally invasive spine surgery for lumbar disc herniation (LDH). Due to its advantages such as lower complications rate, better intraoperative interaction between surgeons and patients, and less risk of exiting nerve root injury, local anesthesia is regarded as one of the merits of PTED.[1] However, it is undeniable that patients who received PTED under local anesthesia could probably experience intense intraoperative pain.

Multiple methods have been adopted to solve this problem. For example, intravenous sedative drugs such as propofol and midazolam are frequently used to keep the patient under light to moderate sedation.[2–5] Considering the adverse effects such as cardiorespiratory depression, the sedation depth should be monitored carefully during the surgery. Intrathecal or general anesthesia is not routinely adopted for the potential risk of nerve injury during the PTED procedure.

Morphine, one of the most classic opioids, has been frequently used in clinics to relieve moderate-to-severe pain. Preoperative administration of morphine could reduce the physiological consequences of nociceptive transmission provoked by invasive procedures, and alleviate the patients' postoperative pain.[6] Compared with short-acting opioids such as fentanyl, a single injection of morphine, which has a half-life of 1.5 hours,[7] can provide long enough analgesic effect for PTED surgery.

Furthermore, it is much more convenient and safer than adopting sedative drugs for morphine's relatively slight effect on patients' respiratory and circulatory function.

The purpose of the current study is to find a safe and effective method to alleviate the intense pain during PTED for LDH under local anesthesia. Therefore, we analyzed the analgesia efficiency and safety of preoperative administration of morphine for PTED.

2. Methods

This clinical observation study was approved by institutional review board of Shanghai Tenth People's Hospital. As the study results obey the normal distribution with a sample size ≥30, we decided to choose about 30 patients for each group. The current study retrospectively analyzed 63 LDH patients treated by PTED in our department from February 2016 to August 2016. The inclusion criteria for LDH are listed as follows: low back pain and sciatica history, imaging findings confirmed LDH, failed in standard conservative treatment for at least 3 months. The exclusion criteria included the following: radiographic findings do not consistent with clinical symptoms or signs, highly free or multilevel LDH, LDH associated with lumbar instability, severe spinal canal stenosis, cauda equina syndrome, or other spinal diseases, severe obesity or underweight, severe mental illness or opioid drugs abuse history, and other severe underlying disease.

Before May 2016, PTED surgery was routinely carried out without any preoperative intervention and there were 32 patients who received PTED surgery during this period. These patients were defined as Group A. Preoperative intramuscular injection of 5 mg morphine became a routine preparation for PTED since May 2016 in our department. There were 31 patients who received intramuscular injection of 5 mg morphine before PTED surgery from May to August and they were defined as Group B. All patients had signed an informed consent. Morphine injection was normally performed before the patients were brought to the operating room. It would take about 30 minutes from the injection to the start of the surgery. Drugs such as Naloxone (Xinhua Pharm, Shandong, China) were routinely prepared as a precaution for severe side effects of morphine.

All patients were followed up in the outpatient department for at least 3 months after their operations.

2.1. Surgery procedure

In this study, all patients were hospitalized for the operation and treated by the same medical team. Patients were placed on the radiolucent operating table in a prone position. The vital signs of patients were monitored carefully during the surgery.

Following the method described by Fan et al, [8] the surface location and puncture strategy was routinely carried out with the help of a localization system. After the puncture target and trajectory were identified, an assigned surgeon infiltrated both skin entry point and deep tissue with about 20 mL 0.1% lidocaine. Following the designed trajectory, an 18G puncture needle was inserted into the puncture target. Additional 5 mL 0.1% lidocaine was routinely infiltrated near the target area. Then, TOM shidi needle was needed to adjust the trajectory to the ideal position. After that, an 8-mm skin incision was made and dilation was performed over the guidewire to stretch the soft tissue. While keeping the guidewire in position, foraminoplasty was performed using a 4-mm drill and then, successively, 6-mm and 8-mm drills to enlarge the intervertebral foramina. Sometimes, a 9-mm drill was needed to further enlarge the

foramina. The following procedure was working cannula placement, which usually needed a hammer to anchor the working cannula into the foramina. After the cannula's position was confirmed by X-ray image, the endoscope was introduced. In order to avoid unwanted procedural pain, large fragments, which were likely to be jammed under or over the nerve root, should be removed piece by piece. The decompression was considered sufficient when all the herniated mass was removed and pulsation of the dural sac was confirmed under the endoscopic view. One stitch was usually enough to close the skin incision.

2.2. Data collection

In our department, patients' maximum leg and back pain was routinely measured by 10 points visual analogue scale (VAS) during pre-, intra-, and postoperation. The VAS score range from 0 to 10, and 0 means no pain while 10 represents the worst pain ever experienced. Both leg and back VAS scores were collected and compared during the following periods. T1: admission to hospital (without any treatment); T2: preparation in the operation room (before any invasive procedures such as puncture or local anesthesia. The analgesic effect of morphine in Group B should be onset during this period); T3: the puncture and dilation; T4: foraminoplasty; T5: the working cannula placement; T6: decompression procedures under endoscopic; T7: 1 hour after surgery; T8: 24 hours after surgery; T9: 3 months after surgery.

Furthermore, patients were asked to grade their experiences of surgery and anesthesia on a 5-point Likert-type scale when they returned to the ward. The Likert-type scale range from 1 to 5, 1 means a very bad experience while 5 indicates a very good experience.[9] At the third month of follow-up, Modified Mac Nab Criteria were used to evaluate the surgical outcomes.

2.3. Statistical analyses

Except for the Statistical Power was calculated using G*Power (version 3.1; Heinrich Heine University, Düsseldorf, Germany), the rest statistical analyses were performed using SPSS (version 21.0; IBM Corp., Chicago, IL). Results were presented as mean ± SD. Chi-square test was used to analyze the differences of categorical variables, such as demographic data, incidence of complications and patients' satisfaction. t test was used to compare the difference of VAS scores between the 2 groups at different periods. $P < .05$ was regarded as statistically significant.

3. Results

There were 32 patients in Group A, with 17 males and 15 females. The average age of this group was 37.72 ± 13.23 years (range, 18–67 years). There were 31 patients in Group B, with 13 males and 18 females. The average age of this group was 41.03 ± 12.84 years (range, 16–63 years). There was no statistical difference in the demographic data between groups (age, $P = .33$; gender, $P = .37$; Table 1).

Both leg and back VAS scores of the 2 groups are listed in Table 2. The preoperative VAS scores showed no significant difference between the 2 groups (leg VAS, $P = .13$; back VAS, $P = .17$). The surgery was regarded effective, as the leg VAS scores in both groups decreased immediately after PTED (Group A, $P < .001$; Group B, $P < .001$). Both leg and back VAS scores of Group B during the surgery were significantly reduced than Group A (Figs. 1 and 2). However, patients in Group B would still

Table 1

Demographic characteristics of the 2 groups.

Variables	Group A	Group B	*P*
Age, y	37.72 ± 13.23	41.03 ± 12.84	.33
Gender (male: female)	17:15	13:18	.37
Surgical segment			.54
L4/L5	19	16	—
L5/S1	13	15	—

Figure 1. Preoperative intramuscular injection of morphine could reduce patients' leg pain during PTED surgery. *Represents a statistical difference ($P < .05$).

suffer medium to severe pain especially during foraminoplasty, working cannula insertion, and decompression. But they could tolerate the pain much easier than the control group. In the third month of follow-up, leg VAS scores were significantly improved in all groups (Group A, $P < .001$; Group B, $P < .001$). Both leg and back postoperative VAS scores between groups were similar at the third month (leg VAS, $P = .48$; back VAS, $P = .35$). This indicated that the preoperative administration of morphine did not influence the pain alleviation of PTED surgery.

The vital signs of patients were stable and no complication such as cardiorespiratory depression occurred. And no additional sedative drugs such as propofol were needed for both groups. There was 1 case of dural tear in Group A, 1 case of superficial infection, and 1 case of residual disc in Group B. Because the dural laceration was too small, repair was unnecessary and the patient received a good recovery. After intramuscular injection of 5 mg morphine, 4 patients in Group B complained nausea and 2 of them experienced vomiting. No other complications such as respiratory depression, bradycardia, pruritus, and constipation were observed. As the adverse reactions were mild and tolerable, drugs were not necessary and the operation could be continued after a rest. All patients fulfilled the survey and no loss of the participants occurred.

The patients' subjective satisfaction of the surgery and anesthesia is demonstrated in Fig. 3. Thirteen patients (40.63%) in Group A regarded the experience of both surgery and anesthesia as satisfied according to Likert-type Scale (graded the experience as very good, good, or neutral). There were 20 patients (64.52%) in Group B who graded the experience as satisfied. According to Modified Mac Nab Criteria, the outcome of Group A at the third month of follow-up was excellent in 4
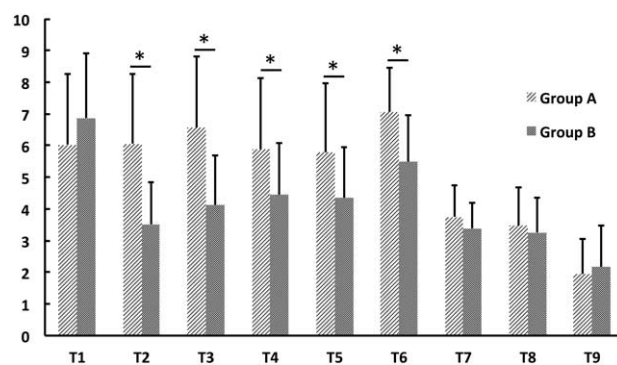
patients (12.5%), good in 22 patients (68.75%), and fair in 6 patients (18.75%). In Group B, the outcome at the third month of follow-up was excellent in 4 patients (12.90%), good in 19 patients (61.29%), fair in 7 patients (22.58%), and poor in 1 patient (3.23%). The surgical outcomes of both groups were good (Fig. 4).

4. Discussion

Nowadays, PTED have brought great benefits to LDH patients, such as slight trauma, no nerve or muscular traction, mild postoperative pain, and quick recovery.[10,11] As is routinely recommended for the PTED surgery, local anesthesia allows patients to communicate or even move their limbs freely under the direction of surgeon during the operation. The patients' feedback such as limb pain or numbness can warn surgeon that adjustment should be made to avoid the potential nerve injury.[10,12,13] Furthermore, due to the regional administration of anesthetic drugs, local anesthesia has little disturbance to the patients' respiratory, circulatory, and other systems. Therefore, patients who cannot tolerate intrathecal or general anesthesia can benefit from PTED.[1] Besides, compared with intrathecal or general anesthesia, local anesthesia can be performed without the anesthetist's help and is much cheaper and more convenient. The

Table 2

The Leg VAS and Back VAS scores of both groups at different time points.

	T1	T2	T3	T4	T5	T6	T7	T8	T9
Leg VAS									
Group A	6.03 ± 2.25	6.06 ± 2.24	6.56 ± 2.30	5.88 ± 2.28	5.78 ± 2.21	7.06 ± 1.41	3.75 ± 1.01	3.47 ± 1.24	1.94 ± 1.13
95% CI	5.22–6.84	5.25–6.87	5.73–7.39	5.05–6.70	4.98–6.58	6.55–7.57	3.38–4.12	3.02–3.92	1.53–2.35
Group B	6.87 ± 2.06	3.52 ± 1.34	4.13 ± 1.59	4.45 ± 1.67	4.35 ± 1.62	5.48 ± 1.50	3.89 ± 0.80	3.26 ± 1.12	2.16 ± 1.34
95% CI	6.11–7.63	3.03–4.01	3.55–4.71	3.84–5.06	3.76–4.95	4.93–6.04	3.09–3.68	2.85–3.67	1.67–2.65
ES	0.37	1.34	1.06	0.62	0.65	1.12	0.36	0.17	0.20
SP	0.30	1.00	0.99	0.68	0.72	0.99	0.29	0.10	0.12
Back VAS									
Group A	1.56 ± 1.39	1.34 ± 1.31	4.31 ± 1.06	8.09 ± 1.20	7.28 ± 1.40	4.97 ± 1.23	3.34 ± 0.83	2.28 ± 1.11	1.81 ± 1.06
95% CI	1.06–2.06	0.87–1.82	3.93–4.69	7.66–8.53	6.78–7.78	4.53–5.41	3.05–3.64	1.88–2.68	1.43–2.19
Group B	2.06 ± 1.46	0.58 ± 0.81	2.42 ± 0.76	6.58 ± 1.54	6.06 ± 1.53	3.52 ± 0.96	2.87 ± 1.06	2.61 ± 0.80	2.06 ± 1.06
95% CI	1.53–2.60	0.28–0.88	2.14–2.70	6.01–7.15	5.50–6.62	3.16–3.87	2.48–3.26	2.32–2.91	1.67–2.45
ES	0.36	0.58	1.78	1.26	0.87	1.18	0.57	0.30	0.24
SP	0.29	0.62	1.00	1.00	0.92	1.00	0.60	0.22	0.16

95% CI = 95% Confidence interval, Back VAS = VAS scores of back pain, ES = effect size, Group A = no preoperative interference, Group B = preoperative intramuscular injection of 5 mg morphine, Leg VAS = VAS scores of leg pain, SP = statistical power, T1 = admission to hospital, T2 = preparation in the operation room, T3 = the puncture and dilation, T4 = foraminoplasty, T5 = the working cannula placement, T6 = decompression procedures under endoscopic, T7 = 1 hour after surgery, T8 = 24 h after surgery, T9 = 3 mo after surgery.
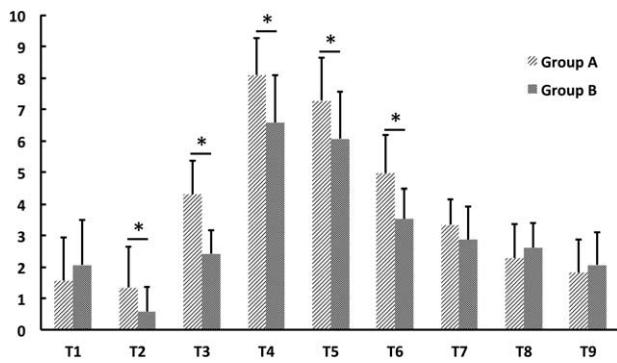
Figure 2. Preoperative intramuscular injection of morphine could reduce patients' back pain during PTED surgery. *Represents a statistical difference (P < .05).
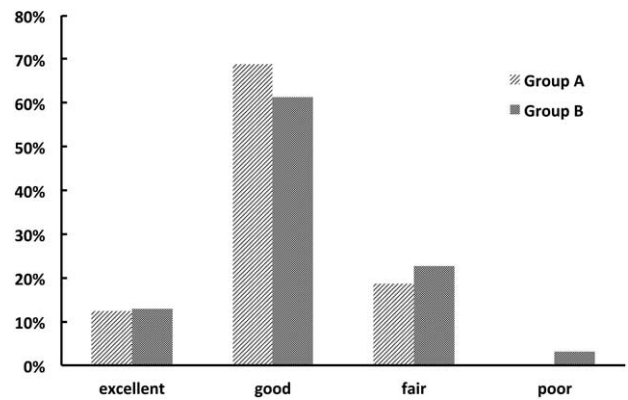
Figure 4. Modified Mac Nab Criteria results between the 2 groups at the third month of follow-up were similar.

introduction of foraminoplasty has expanded the application of PTED, but it may magnify the intraoperative pain under local anesthesia. Normally, PTED can be completed under local anesthesia, but patients have to endure the intense intraoperative pain.

The present study demonstrated that preoperative intramuscular injection of morphine could significantly alleviate the intraoperative pain of PTED. We observed that patients would still surfer moderate to severe pain, especially during foraminoplasty, working cannula insertion, and decompression. But as far as we concern, this method could reduce the intensity of intraoperative pain to a level patients could tolerate easier. Actually, patients who received preoperative injection of morphine were more satisfied with the surgery and anesthesia than these who did not. Except for a higher incidence of nausea and vomiting in Group B, there was no significant difference between the 2 groups with regard to incidences of neurological complications, surgical result, etc. The safety of this anesthesia strategy was good.

Morphine, which is hydrophilic opioids with a half-life of about 1.5 hours, has a longer lasting action than lipophilic opioids such as fentanyl.[7,14] Preoperative use of morphine, similar to the concept of preemptive analgesia, can reduce the physiological consequences of nociceptive transmission provoked by incision and other invasive manipulations.[15,16] Furthermore, longer lasting action makes morphine suitable for this anesthesia strategy, as its analgesic effect is more likely to last till the end of the surgery. In addition, intramuscular injection

of morphine is much more convenient and cheaper than adopting sedative drugs or intrathecal anesthesia. Due to the wide distribution of opioid receptors, morphine has a broad spectrum of adverse effects, such as respiratory depression, constipation, cardiovascular disorders, nausea, vomiting, etc. In this study, limited dosage and intramuscular injection were adopted as precautions to reduce morphine's adverse effects.[17,18] Actually, the incidence of adverse effects was relatively low and no severe complications occurred in the present study. Opioid-induced hyperalgesia (OIH), which is defined as a state of nociceptive sensitization after exposure to opioids, is another issue to consider when choosing morphine as a preoperative interference.[18,19] Because long-term and high doses of potent opioids are regarded as the common causes, OIH is less likely happen in this anesthesia strategy. Moreover, no hyperalgesia was observed in the present study.

Another method to reduce the intraoperative pain is to keep patients under light to moderate sedation by administering sedative drugs.[4,20] Propofol, the most widely used sedative drug for its rapid onset and offset, can induce sedation by acting on γ-aminobutyric acid subtype A (GABA$_A$) receptors in the central nervous system and other tissues.[21] However, due to its adverse effects such as cardiorespiratory depression, a professional anesthetist is required to monitor the patient's vital signs during the operation. In the studies reported by Hoogland et al,[11,20] intravenous analgesia with opioid medication and midazolam sedation were used to enhance the effect of local anesthesia. However, neither patients' subjective experience nor the anesthesia-related complications were mentioned in their study. Midazolam, one of benzodiazepines, can produce sedative hypnotic, anxiolytic, and muscle relaxant effects.[22] Compared with propofol, midazolam is much safer due to its advantage in lower incidence of cardiorespiratory depression.[22] But it shows significant disadvantages regarding to time of onset and offset.[21] Interestingly, a Cochrane review found that there was low-quality evidence that intravenous midazolam administered before a procedure reduced anxiety when compared with placebo.[23] Therefore, further studies are needed to evaluate the effect of intraoperative administration of sedative drugs in PTED surgery.

In certain patients who are not satisfied with local anesthesia, intrathecal anesthesia might be a good choice.[13,24,25] Epidural anesthesia with limited concentration and dosage of anesthetic can effectively block sensation and preserve lower limb motor function. Some studies demonstrated that epidural anesthesia could significantly reduce the intraoperative pain of PTED
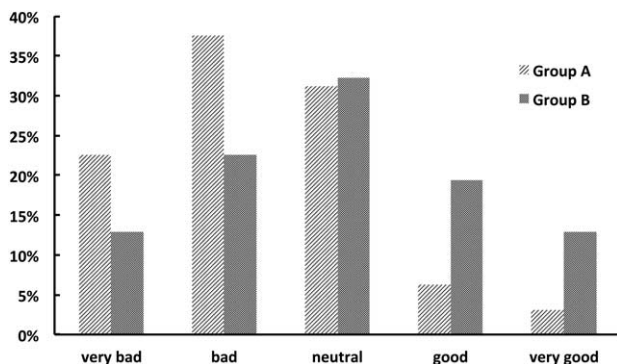
Figure 3. Patients who received preoperative administration of morphine were more satisfied with the surgery and anesthesia experience.

without increasing neurological complications.[13] However, considering the patients' sensation is blocked, they are unable to sense the pain immediately under epidural anesthesia. It is not until the motor dysfunction has displayed that we can realize the nerve is injured. Therefore, intrathecal anesthesia should not be the first choice for PTED.

There are several limitations of this strategy. For one thing, this is a retrospective study with a small sample size. High-quality randomized controlled trials are needed to further demonstrate the effect of this strategy. For another, morphine has a broad spectrum of adverse effects. Efforts should be devoted to make the best use of morphine's advantages and bypass its disadvantages. Furthermore, even though morphine could alleviate patients' intraoperative pain, comparing studies between different opioids or sedative drugs or anesthesia methods should be carried out to find an ideal anesthesia strategy for PTED.

5. Conclusion

Preoperative intramuscular injection of morphine could reduce the patients' pain during the PTED surgery and improve the patients' satisfaction without affecting the surgical outcome. Except for a higher incidence of nausea and vomiting, this method is relatively safe and convenient.

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