

# Effect of low-dose lidocaine on MEPs in patients undergoing intracranial tumor resection with propofol anesthesia

## A randomized controlled trial

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### Abstract

**Objective:** To investigate the effect of low-dose lidocaine on motor evoked potentials (MEPs) in patients undergoing intracranial tumor resection with propofol anesthesia.

**Methods:** Forty patients who underwent intracranial tumor resection and required MEP monitoring were selected. They were randomly divided into the lidocaine group (group L, n = 20) and the control group (group C, n = 20) by computer-generated randomization. All patients were given propofol anesthesia under the guidance of the bispectral index. In group L, 1 mg/kg of lidocaine was injected intravenously during anesthesia induction. Then, lidocaine was continuously pumped at a speed of 1 mg/kg/h until the operation started. Group C was given an equal volume of normal saline. Heart rate (HR), mean artery pressure (MAP), and bispectral index were recorded before anesthesia induction (T0), 2 minutes after tracheal intubation (T1), and 35 minutes (T2), and 50 minutes (T3) after anesthesia induction. The amplitude and latency of MEP at T2 and T3, the total dosage of propofol after anesthesia induction, and adverse events before T3 were recorded.

**Results:** Compared with those in group C, HR and MAP were significantly decreased at T1 in group L. No significant differences were observed in HR and MAP at T0, T2, and T3 between group L and group C. The total dosage of propofol and the incidence of adverse events were significantly lower in group L than in group C before T3. There were no significant differences in the amplitude and latency of MEP between the 2 groups at each time point.

**Conclusions:** Low-dose lidocaine has no obvious effect on MEP in patients undergoing intracranial tumor resection. However, it increased hemodynamic stability, reduced propofol use, and decreased the incidence of adverse events.

**Abbreviations:** ASA = American Society of Anesthesiologists, BIS = bispectral index, HR = heart rate, MAP = mean artery pressure, MEP = motor evoked potential, PetCO<sub>2</sub> = the end-expiratory carbon dioxide partial pressure, TIVA = total intravenous anesthesia.

**Keywords:** intracranial tumor resection, lidocaine, motor evoked potentials, propofol

## 1. Introduction

Intracranial tumors are considered one of the most feared tumors because their presence may lead to severe disability and physical dysfunction.<sup>[1]</sup> At present, intracranial tumors are commonly treated by surgery. Motor evoked potential (MEP) monitoring can effectively reduce the occurrence of postoperative neurological complications and improve the overall tumor resection rate.<sup>[2]</sup> However, MEP monitoring is easily affected by surgical procedures, anesthetic drug use, and other factors. A Delphi consensus indicates that total intravenous anesthesia (TIVA) is the

most reliable anesthesia method to obtain high-quality MEP signals. Propofol, the most commonly used drug in TIVA, inhibits MEP signals in a dose-dependent manner. Maintaining low-dose propofol infusion by adding adjuvant drugs is considered to be beneficial for good MEP signal acquisition.<sup>[3]</sup> Previous studies have shown that injection of low-dose lidocaine reduces the use of propofol during TIVA.<sup>[4]</sup> However, there is no evidence that reduced propofol by low-dose lidocaine injection can improve MEP monitoring. In the present study, we explore the effect of low-dose lidocaine on MEP in patients undergoing intracranial tumor resection with propofol anesthesia.

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*The datasets generated and analyzed during the current study are not publicly available due to institutional restrictions but are available from the corresponding author on reasonable request. If required, contact lmj0524@163.com.*

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## 2. Materials and methods

This study was approved by the Medical Ethics Committee of the Brain Hospital Affiliated to Nanjing Medical University (2020-KY119-02). Moreover, it was registered in the Chinese Clinical Trial Register (ChiCTR2100053218). The study protocol followed the CONSORT guidelines. The study protocol was performed according to the relevant guidelines. Written informed consent was obtained from patients and their families.

### 2.1. Subjects

Patients who underwent intracranial tumor resection and required MEP monitoring at the Brain Hospital Affiliated to Nanjing Medical University from November 2021 to March 2022 were eligible for inclusion. The inclusion criteria were as follows: age range, 18 to 65 years; American Society of Anesthesiologists grade, I to II; and body mass index, 18.5 to 30 kg/m<sup>2</sup>. The exclusion criteria were lidocaine allergy; contraindication to transcranial electrical stimulation; neuromuscular transmission dysfunction; neuropsychosis or the use of corresponding drugs; diabetes mellitus with peripheral nerve ending lesions; and severe heart, lung, liver, and kidney dysfunction.

### 2.2. Sample size calculation

The sample size was calculated by G-Power software (version 3.1). Based on the preexperimental results, the dosage of propofol was 256.00 ± 19.14 mg in group L and 280.00 ± 27.24 mg in group C. The test level  $\alpha$  was taken as 0.05. The power level, 1- $\beta$ , was taken as 0.8. Therefore, a sample size of 14 was required in each group. Considering the rate of withdrawal (-15%), the final sample size for each group was 20.

### 2.3. Anesthesia preparation

All patients maintained the NPO protocol before the operation. After entering the operating room, electrocardiogram, noninvasive arterial blood pressure, peripheral oxygen saturation, and bispectral index (BIS), as provided by Aspect Medical Systems, were monitored.

### 2.4. Anesthesia induction

Midazolam injection 0.05 mg/kg, propofol injection 1.5 mg/kg, sufentanil citrate injection 0.3  $\mu$ g/kg, and cis-atracurium besylate injection 0.1 mg/kg were used for anesthesia induction. In group L, lidocaine hydrochloride injection (1 mg/kg) was administered during induction; in group C, an equal volume of normal saline was given. Endotracheal intubation and mechanical ventilation were performed after the above drugs took effect. The end-expiratory carbon dioxide partial pressure (PetCO<sub>2</sub>) was maintained between 30 and 35 mm Hg. The BIS value was maintained between 40 and 60.

### 2.5. Anesthesia maintenance

After endotracheal intubation, both groups continued to pump propofol 4 to 12 mg/kg/h, under the guidance of BIS, until the end of the operation. In group L, lidocaine 1 mg/kg/h was continuously pumped until the operation started, while in group C, an equal volume of normal saline was continuously pumped. In both groups, 10  $\mu$ g sufentanil was administered intravenously 5 minutes before head fixation and skin incision. Cis-atracurium 1  $\mu$ g/kg/min and remifentanil 0.05 to 0.3  $\mu$ g/kg/min were pumped 50 minutes after induction.

### 2.6. MEP monitoring

An Endeavor® neuroelectrophysiological monitor, manufactured by the American Nicolet company, was used for MEP monitoring. After anesthesia induction, disposable sterile needles punctured the patient's muscles. Then, the muscle was selected as the recording electrode. MEP was induced through transcranial electrical stimulation with 5 short pulses: stimulation interval, 0.1 ms, and stimulation intensity, 150 V.

### 2.7. Observation indices

Heart rate (HR), mean artery pressure (MAP), and BIS before anesthesia induction (T0), 2 minutes after tracheal intubation (T1), 35 minutes (T2), and 50 minutes (T3) after anesthesia induction were recorded. The amplitude and latency of MEP at T2 and T3, the total dosage of propofol, and adverse events before T3 were also recorded. Data were recorded by residents who were blinded to the group allocation.

### 2.8. Statistical analysis

Data were analyzed by IBM SPSS Statistics 21.0. The counting data are represented by frequencies or percentages and analyzed by the chi-square test. The measurement data are expressed as the mean ± standard deviation. The HR, MAP, BIS, and MEP of the 2 groups were compared by repeated measurement analysis of variance. The dosage of propofol used in the 2 groups was compared by independent samples *t* test. A *P* value of <.05 was considered statistically significant.

## 3. Results

### 3.1. Baseline characteristics of the study subjects

A total of 40 patients were included in the present study. As shown in Table 1, there were no significant differences in terms of sex, age, weight, or BMI between group L and group C.

### 3.2. Changes in HR, MAP, and BIS

As shown in Tables 2 and 3, compared with those in group C, HR and MAP were significantly lower at T1 in group L. No significant differences were observed in HR and MAP at T0, T2, and T3 between the groups. As shown in Table 4, there was no significant difference in BIS between the groups at each time point.

### 3.3. Comparison of MEP

As shown in Table 5, there were no significant differences in the amplitude and latency of MEP between the 2 groups at each time point.

**Table 1**  
Baseline characteristics of the study subjects.

Parameter	Group L (n = 20)	Group C (n = 20)	<i>P</i> value
Age (yr)	53.00 ± 8.99	52.60 ± 6.66	.87
Male (n)	8	8	1.00
Female (n)	12	12	1.00
BMI (kg/m <sup>2</sup> )	23.53 ± 2.32	23.76 ± 2.55	.75
Weight (kg)	62.05 ± 9.41	63.15 ± 7.01	.97

Data presented as mean ± SD or as number.

BMI = body mass index, SD = standard deviation.

**Table 2****Comparison of HR between group L and group C.**

Group	Group L (n = 20)	Group C (n = 20)	P value
T0	75.75 ± 9.84	79.65 ± 10.22	.74
T1	67.05 ± 5.07	76.15 ± 7.45	.00
T2	70.10 ± 6.66	74.45 ± 10.13	.12
T3	70.55 ± 7.11	75.45 ± 9.46	.07

Data presented as mean ± SD.

HR = heart rate, SD = standard deviation.

**Table 3****Comparison of MAP between group L and group C.**

Group	Group L (n = 20)	Group C (n = 20)	P value
T0	91.75 ± 8.37	91.80 ± 7.61	.98
T1	81.10 ± 6.69	85.20 ± 6.08	.05
T2	83.60 ± 5.17	81.85 ± 4.68	.27
T3	83.40 ± 5.66	82.15 ± 4.67	.45

Data presented as mean ± SD.

MAP = mean artery pressure, SD = standard deviation.

**Table 4****Comparison of BIS between group L and group C.**

Group	Group L (n = 20)	Group C (n = 20)	P value
T0	96.70 ± 1.17	96.40 ± 1.05	.40
T1	43.30 ± 2.25	43.65 ± 2.01	.61
T2	46.60 ± 2.65	47.80 ± 2.55	.16
T3	47.00 ± 2.38	47.35 ± 3.31	.70

Data presented as mean ± SD.

BIS = bispectral index, SD = standard deviation.

**Table 5****Comparison of the amplitude and latency of MEP between group L and group C.**

Parameter	Group	Group L (n = 20)	Group C (n = 20)	P value
Amplitude (μV)	T2	305.26 ± 82.55	321.05 ± 95.39	.59
	T3	311.75 ± 83.88	322.50 ± 86.14	.69
Latency (ms)	T2	17.79 ± 2.07	17.84 ± 2.12	.94
	T3	17.75 ± 1.55	17.80 ± 1.91	.93

Data presented as mean ± SD.

MEP = motor evoked potential, SD = standard deviation.

**3.4. Propofol usage**

The dosage of propofol after anesthesia induction used in Group L was 246.50 ± 27.44 mg, compared with 273.35 ± 33.79 mg in Group C. The total dosage of propofol after anesthesia induction used was significantly less in Group L than in Group C before T3 ( $t = 2.759$ ,  $P = .009$ ).

**3.5. Adverse events**

As shown in Table 6, the incidence of total adverse events (coughing, hypertension, or bradycardia) was significantly lower in group L than in group C before T3.

**4. Discussion**

Optimizing the anesthesia scheme and obtaining satisfactory MEP waveforms is a major task for anesthesiologists utilizing

**Table 6****Comparison of the adverse events between group L and group C.**

Group	Group L (n = 20)	Group C (n = 20)	χ <sup>2</sup>	P value
Coughing	1	2	0.36	.55
Hypertension	1	3	1.11	.29
Bradycardia	0	3	3.24	.07
Incidence	2 (10%)	8 (40%)	4.80	.03

Data presented as frequency and percentage (%).

MEP monitoring in neurosurgery. During the monitoring process of intraoperative MEP, many factors will affect the monitoring results. In addition to narcotic drugs, the depth of anesthesia, surgery, and body temperature will be affected. In this study, the narcotic drugs and depth of anesthesia were adjusted uniformly. Both groups of patients underwent body temperature monitoring and protection to maintain their body temperature at 36°C to 37°C. In order to reduce the interference of surgical factors on the results, the results of this study were collected before the operation. To date, muscle relaxants and inhaled anesthetics have been shown to exert strong inhibitory effects on MEP production. Muscle relaxants act directly on neuromuscular junctions, causing a decrease in the amplitude of MEP and failure of MEP monitoring. Although some studies have shown that MEP signals can be successfully obtained by applying low concentrations of inhaled anesthetics, stronger stimulation is required to induce MEP with inhaled anesthetics than with propofol.<sup>[5]</sup> In the present study, TIVA was, therefore, selected as the anesthesia scheme. To avoid the influence of muscle relaxants on MEP monitoring, cis-atracurium 0.1 mg/kg was given during anesthesia induction. The clinical muscle relaxant maintenance time of cis-atracurium was approximately 30 minutes. Although MEP was not induced at T2 in 1 case in each group, the induction rate of the MEP waveform in both groups at T3 was 100%.

Propofol is often used as an anesthetic in neurosurgery because of its ability to constrict cerebral blood vessels and reduce intracranial pressure. However, propofol inhibits the activity of spinal gray matter α motor neurons and has a dose-dependent inhibitory effect on MEP induction.<sup>[6]</sup> Therefore, we need to reasonably reduce the use of propofol in MEP monitoring during neurosurgery. Previous studies have shown that low-dose lidocaine reduces the use of propofol during general anesthesia.<sup>[4]</sup>

Lidocaine is widely used in the clinic as a common medium effect amide local anesthetic. It has a multimodal mechanism of action and can inhibit nociceptive stimulation by blocking channels in the pain transmission pathway, thereby reducing the required dose of propofol and opioids. In 2 studies, small doses of lidocaine at 1 and 1.5 mg/kg were applied. The results showed that lidocaine had no effect on the monitoring results of MEP and somatosensory evoked potential during spinal surgery.<sup>[4,7]</sup> However, lidocaine inhibited the propagation of action potentials and the excitability of neurons by blocking voltage-gated channels. This effect on electroactive cells was considered to interfere with electrophysiological monitoring. Studies have shown that after intravenous injection of 3 mg/kg lidocaine, 4 mg/kg/h continuous influence further reduces the amplitude of somatosensory evoked potential and prolongs the incubation period.<sup>[8]</sup> At present, the mechanism of lidocaine's influence on intraoperative electrophysiological monitoring is not clear, and whether it is related to drug concentration or interaction with other drugs needs to be further studied. Lidocaine inhibits noxious stimulation by blocking sodium channels in the pain conduction pathway to reduce the required dose of propofol and opioids.<sup>[9]</sup> The recommended dose of intravenous lidocaine is 1.0 to 2.0 mg/kg, followed by 1.0 to 2.0 mg/kg/h continuous intravenous injection. However, it is necessary to gradually reduce the continuous infusion rate of lidocaine in surgeries with long durations.<sup>[10]</sup> The duration of neurosurgery is relatively long (>2

hours); therefore, the minimum safe doses of lidocaine that were selected in the present study were 1.0 mg/kg and 1.0 mg/kg/h.

Our results showed that the dosage of propofol in group L was  $246.50 \pm 27.44$  mg; however, the dosage was  $<273.35 \pm 33.79$  mg in group C. Interestingly, no significant differences were observed in MEP amplitude and latency between the 2 groups. We speculated that, first, the reduction in propofol did not reach the threshold that could induce MEP change and, second, the use of lidocaine offset the improvement of MEP signals, which were caused by the reduction in propofol dosage. Further studies will be needed to explore the reasons behind the results.

Intravenous injection of lidocaine produces analgesic, sedative, and anti-inflammatory effects. Moreover, it also inhibits the release of adrenaline and catecholamine and alleviates the stress response caused by a surgical operation.<sup>[11,12]</sup> Studies have shown that intravenous application of 1.5 mg/kg lidocaine reduces hemodynamic changes during endotracheal intubation, extubation, and operation.<sup>[13]</sup> Our results showed that MAP decreased at T1 in both groups; however, it was significantly decreased in group L but not in group C. HR decreased at T1 in group L. These results indicate that low-dose lidocaine reduces the stress response caused by endotracheal intubation. Moreover, lidocaine has a good effect on maintaining hemodynamic stability. In the present study, the incidence of adverse events (hypertension, bradycardia) was significantly lower in group L than in group C.

A small dose of lidocaine was used in this study, and no allergic or toxic reactions occurred during the study period. However, this test has a small sample size, and there is no continuous infusion of lidocaine throughout the operation. Therefore, the safety of continuous application in long-term operations needs further verification and theoretical discussion. Since most narcotic drugs have different effects on MEP monitoring, the controllability of the combined application of multiple narcotic drugs is reduced due to the interaction between drugs, thus affecting the reliability of the research results.

In summary, in intracranial tumor resection, 1.0 mg/kg followed by 1.0 mg/kg/h (<6 hours) continuous intravenous injection of low-dose lidocaine had no significant effect on MEP monitoring results. Lidocaine reduces the use of propofol, inhibits endotracheal intubation reactions, maintains hemodynamic stability, and reduces the incidence of adverse reactions. It is recommended to use lidocaine in MEP monitoring of intracranial tumor resection.

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