

Effect of Low-dose Lidocaine on Motor Evoked Potentials in Patients Undergoing Intracranial Tumor Resection With Propofol Anesthesia

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Abstract

Object

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

Methods

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

Results

Compared with Group C, HR and MAP were significantly decreased at T1 in Group L. No significant difference was 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 was no significant difference in the amplitude and latency of MEP between the two groups at each time point.

Conclusion

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

Introduction

Intracranial tumors are considered one of the most feared tumors, which may lead to severe disability and physical dysfunction (1). At present, intracranial tumors are commonly treated by surgery. Motor evoked potentials (MEP) monitoring can effectively reduce the occurrence of postoperative neurological complications and improve the overall tumor resection rate (2). However, MEP monitoring is easily affected by surgical procedures, anesthetic drugs, 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.(3) Previous studies have shown that injection of low-dose lidocaine reduces the use of propofol during TIVA.(4) However, there is no evidence that reduced propofol by low-dose lidocaine injection can improve MEP monitoring. In the present study, we intend to explore the effect of low-dose lidocaine on MEP in patients undergoing intracranial tumor resection with propofol anesthesia. We hope to provide some reference for clinical medicine.

Materials And Methods

This study has been approved by the Medical Ethics Committee of the Brain Hospital Affiliated to Nanjing Medical University (2020-KY119-02). And it also has been registered at <http://www.chictr.org.cn> (15/11/2021,ChiCTR2100053218) . The study protocol followed the CONSORT guidelines. The study protocol was performed in the relevant guidelines.Written informed consent was obtained from patients and their families.

Subjects

Patients undergoing intracranial tumor resection and required MEP monitoring at the Brain Hospital Affiliated to Nanjing Medical University from June 1, 2020 to July 30, 2021 were eligible for inclusion. Inclusion criteria were: age range, 18 to 65 years; American Society of Anesthesiologists (ASA) grade, I to II; and Body Mass Index, 18.5 to 30. 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.

Sample size calculation

The sample size is calculated by G-Power software (version 3.1). Based on the pre-experimental 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 α 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. Taking into account the rate of withdrawal (-15%), the final sample size for each group was 20.

Anesthesia preparation

All patients were given fasting and drinking before operation. After entering the operating room, electrocardiogram, noninvasive arterial blood pressure, peripheral oxygen saturation, and bispectral index (BIS) were monitored.

Anesthesia induction

Midazolam 0.05 mg/kg, propofol 1.5mg/kg, sufentanil 0.3ug/kg, and cis-atracurium 0.1 mg/kg were used for anesthesia induction. In Group L, lidocaine 1 mg/kg was administered during induction; in Group C, 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 (PetCO₂) was maintained between 30 and 35 mmHg. The BIS value was maintained between 40 and 60.

Anesthesia maintenance:

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

MEP monitoring

Endevor® neuroelectrophysiological monitor was used for MEP monitoring. After anesthesia induction, disposable sterile needles were punctured into the patient's muscles. Thenar muscle was selected as the recording electrode. MEP was induced through transcranial electrical stimulation with 5 short pulses: stimulation interval, 0.1 ms; stimulation intensity, 150V.

Observation indices

Heart rate (HR), mean artery pressure (MAP) and BIS before anesthesia induction (T0), 2 min after tracheal intubation (T1), 35 min (T2) and 50 min (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.

Statistical analysis

Data were analyzed by SPSS 21.0. The counting data are represented by frequencies or percentages and analyzed by chi-square test. The measurement data are expressed as the mean ± standard deviation (SD). The HR, MAP, BIS, and MEP of the two groups were compared by repeated measurement analysis of variance. The dosage of propofol use of the two groups was compared by independent-samples t-test. P<0.05 was considered as statistically significant.

Results

Baseline Characteristics of the study subjects

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

Changes of HR, MAP, and BIS

As showed in Table 2 and 3: Compared with 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 groups. As shown

in Table 4, there was no significant difference in BIS between groups at each time point.

Comparison of MEP

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

Propofol usage

The dosage of propofol use in Group L was 246.50 ± 27.44 mg, compared with 273.35 ± 33.79 mg in Group C. The total dosage of propofol use was significantly decreased in Group L than in Group C before T3 ($t=2.759$, $P=0.009$).

Adverse events

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

Discussion

Optimizing anesthesia scheme and obtaining satisfactory MEP waveforms is one of the tasks of anesthesiologists in neurosurgery under MEP monitoring. 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 the application of low concentration of inhaled anesthetics, a stronger stimulation is required to induce MEP in inhaled anesthetics than propofol.(5) In the present study, TIVA was therefore selected as the anesthesia scheme. In order to avoid the influence of muscle relaxants on MEP monitoring, cis-atracurium 0.1mg/kg was given during anesthesia induction. The clinical muscle relaxant maintenance time of cis-atracurium was about 30 minutes. Although MEP was not induced at T2 on one case in each group, the induction rate of MEP waveform in both groups at T3 was 100%.

Propofol is often used as anesthetics in neurosurgery because of its constriction of cerebral blood vessels and reduction of intracranial pressure. However, propofol inhibits the activity of spinal gray matter α motor neurons and has a dose-dependent inhibitory effect on MEP induction.(6) 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.(4) Lidocaine inhibits noxious stimulation by blocking sodium channels in pain conduction pathway, so as to reduce the dose of propofol and opioids.(7) The recommended dose of intravenous lidocaine is 1.0-2.0 mg/kg, followed by 1.0-2.0 mg/kg·h continuous intravenous injection. However, it is needed to gradually reduce the continuous infusion rate of lidocaine in a long-term surgery.(8) The duration of neurosurgery is relatively long (>2 hours); therefore, the minimum safe dose of lidocaine 1.0 mg/kg and 1.0 mg/kg·h was selected in the present study. Our results showed that the dosage of propofol in Group L was $246.50 \pm$

27.44mg, which was less than 273.35 ± 33.79 mg in Group C. Interestingly, no significant difference was observed in MEP amplitude and latency between the two groups. We speculated that: first, the reduction in propofol did not reach the threshold which could induce MEP change; Second, lidocaine offset the improvement of MEP signal caused by the reduction in propofol. Further studies will be needed to explore the reasons.

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 surgical operation.(9, 10) Studies have shown that intravenous application of 1.5mg/kg lidocaine reduces hemodynamic changes during endotracheal intubation, extubation, and operation.(11) Our results showed that MAP decreased at T1 in both groups, however, they were significantly decreased in Group L, 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 of maintaining hemodynamic stability. In the present study, the incidence of adverse events (hypertensive, bradycardia) was significantly lower in Group L than that in Group C.

A small dose of lidocaine was used in the present study. No allergic or toxic reactions were observed throughout the process. The sample size of our study was small and lidocaine was not continuously infused during the operation. Therefore, it needs further verification in the future.

In conclusion, low-dose lidocaine has no obvious effect on MEP during propofol anesthesia, but it reduces the use of propofol, inhibits the reaction to endotracheal intubation, maintains the stability of hemodynamics, and decreases the incidence of adverse reactions. It is recommended that lidocaine can be used during MEP monitoring in intracranial tumor resection surgery.

Declarations

Authors' contributions

Meijuan Liu: Visualization, Investigation, Writing original draft

Ning Wang: Validation, Formal analysis

Dong Wang, Juan Liu: Supervision, Data curation

Wenjie Jin: Conceptualization, Methodology, Writing - review & editing

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Availability of data and materials

The datasets generated and analysed 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.

Consent for publication

Not applicable

Competing interests

All authors declare that they have no conflicts of interest.

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Tables

Table 1, Baseline Characteristics of the Study Subjects [\pm SD, %n=20]

Group	Sex		Age (year)	Weight (kg)	BMI (kg/m ²)
	Male	Female			
Group L	8	12	53.00 \pm 8.76	62.05 \pm 9.41	23.53 \pm 2.32
Group C	8	12	52.60 \pm 6.49	63.15 \pm 7.01	23.78 \pm 2.55

Table 2, Comparison of HR between Group L and Group C [\pm SD, n=20]

Group	T ₀	T ₁	T ₂	T ₃
Group L	73.10 \pm 7.96	75.35 \pm 7.04	71.15 \pm 7.31	71.45 \pm 7.42
Group C	73.30 \pm 7.04	83.85 \pm 7.80 [#]	69.85 \pm 5.82	69.55 \pm 5.05

Group L: * P <0.05, compared with T₀; Group C[#] P <0.05, compared with T₀

Table 3, Comparison of MAP between Group L and Group C [\pm SD, n=20]mmHg]

Group	T ₀	T ₁	T ₂	T ₃
Group L	92.95 \pm 7.73	93.60 \pm 8.98	88.95 \pm 6.97	88.65 \pm 6.88
Group C	91.80 \pm 7.42	98.80 \pm 6.76 [#]	89.20 \pm 6.54	88.90 \pm 6.07

Group L: * P <0.05, compared with T₀; Group C[#] P <0.05, compared with T₀

Table 4, Comparison of BIS between Group L and Group C [\pm SD, n=20]

Group	T ₀	T ₁	T ₂	T ₃
Group L	96.70±1.14	42.60±1.46*	46.60±2.65*	47.00±2.32*
Group C	96.40±1.02	43.65±1.96 [#]	47.80±2.48 [#]	47.35±3.23 [#]

Group L: **P*<0.05, compared with T₀; Group C[#]*P*<0.05, compared with T₀

Table 5, Comparison of the amplitude and latency of MEP between Group L and Group C [±SD, n=20]

Group	amplitude [μV]		latency [ms]	
	T ₂	T ₃	T ₂	T ₃
Group L	296.36±69.29	271.75±69.95	17.36±2.02	17.75±1.51
Group C	300.00±79.58	303.00±67.61	17.47±2.03	17.80±1.86

Table 6, Comparison of the adverse events between Group L and Group C [n% n=20]

Group	Coughing	hypertension	Bradycardia	Incidence
Group L	1	1	0	2 [10.00]
Group C	2	3	3	8 [40.00]