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SHORT COMMUNICATION

Lidocaine pretreatment reduces the frequency and severity of myoclonus induced by etomidate

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Abstract The objective of this study was to assess the effects of lidocaine on the incidence and severity of myoclonic movements induced by etomidate. Sixty patients were randomly assigned to receive either 20 mg lidocaine or saline ($n = 30$, each), 30 s before administration of etomidate (0.3 mg/kg). One minute after etomidate administration we assessed severity of myoclonus. Pretreatment with lidocaine significantly reduced both the incidence and severity of myoclonic movements. As a conclusion, lidocaine is an effective and safe drug to reduce the etomidate-induced myoclonus without significant side effects.

Keywords Etomidate · Lidocaine · Myoclonus

Etomidate is a hypnotic agent with a stable cardiovascular profile and minimal respiratory side effects. Therefore, etomidate is a frequently preferred agent for hemodynamically unstable patients [1]. However, etomidate formulated with propylene glycol is associated with side effects including injection pain and myoclonus [2, 3]. Although the problem of pain on injection has been solved by the lipid formulation for etomidate (Etomidate-Lipuro; Braun, Melsungen, Germany) [4], the problem of etomidate-induced myoclonus has not been solved [5].

Although the mechanism of the myoclonus is not clear, benzodiazepines, opioids, and rocuronium have been used as pretreatments to reduce etomidate-induced myoclonus [6–10]. However, no published data are yet available about the effects of lidocaine on myoclonus after injection of etomidate.

The objective of this study was to assess the effects of pretreatment with lidocaine on the incidence and severity of myoclonic movements due to etomidate.

This prospective, randomized, double-blind controlled study was approved by the Institutional Ethics Committee of Ministry of Health Diskapi Yildirim Beyazit Educational and Research Hospital. Sixty adult, ASA physical status I or II patients undergoing general anesthesia for elective orthopedic and general surgical procedures were included in the study. No premedication was given to patients.

Patients with adrenal cortex dysfunction [11], neurologic disease, psychiatric disorders, drug allergy, or who had received sedatives, analgesics, or opioids within the previous 24 h were excluded from the study.

Patients were randomly assigned to one of two groups to receive either 1 ml (20 mg) lidocaine ($n = 30$; Group L) or 1 ml saline ($n = 30$; Group S). Randomization was provided by use of shuffled, sealed, opaque, numbered envelopes.

On arrival at the operating room, standard monitoring was applied and a 20-gauge cannula was inserted into a vein on the dorsum of the patient's nondominant hand and infusion of 0.9% saline at 1.5 ml/kg/h was started.

Patients in group L received 1 ml lidocaine 2% (20 mg) and patients in group S received 1 ml normal saline. After preoxygenation, both agents were given intravenously over 30 s just before anesthesia induction. For anesthesia induction 0.3 mg/kg etomidate was injected over a period of 1 min. Patients were observed continuously for myoclonus by a physician who was blinded to treatment group. Myoclonic movements were defined as involuntary short

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contraction of muscles leading to a short observable movement of body parts. The intensity of myoclonus was graded as: 0, no myoclonus; 1, mild myoclonus (short movements of a body segment e.g. a finger or a wrist only), 2, moderate myoclonus (mild movements of two different muscles e.g. face and leg); or 3, severe myoclonus (intense clonic movements in two or more muscle groups, fast adduction of a limb) [12, 13]. One minute after administration of the induction agent and evaluation of myoclonus, vecuronium 0.1 mg/kg was given to facilitate tracheal intubation. After intubation, anesthesia was maintained with sevoflurane in a mixture of nitrous oxide in oxygen.

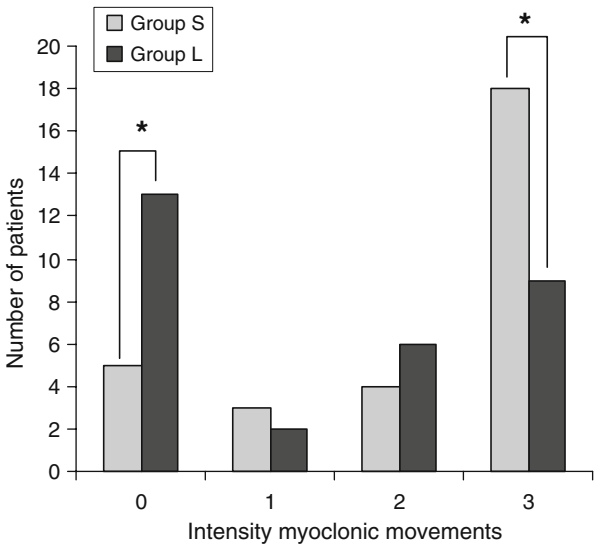
A sample size of 30 patients per group was estimated to provide 80% power to detect a reduction rate of 0.4 at the incidence of myoclonus in treatment group, using a power analysis with $\alpha = 0.05$. Data are presented as number of patients for categorical variables or mean ± standard deviation. Statistical analysis was performed with SPSS 14.0. Demographic data were analyzed using Student's *t* test. Fisher's exact test was used to compare categorical variables among the groups. Correlation analysis was based on Pearson's *r*. Results were considered statistically significant when $p < 0.05$.

There were no significant differences between the two groups in age (51.5 ± 13 and 53.7 ± 11), body mass index (24.1 ± 3.4 and 23.2 ± 3.1), gender (M/F: 17/13 and 14/16), or ASA physical status (I/II: 21/9 and 20/10).

Pretreatment with lidocaine significantly reduced both the incidence and severity of myoclonic movements after induction with etomidate ($p < 0.01$). Myoclonus was observed in 25 patients in group S and 17 in group L. Severe myoclonus was observed for 18 patients in group S and 9 in group L (Fig 1).

The main finding of this study was that use of 20 mg lidocaine before etomidate injection reduced the incidence and severity of myoclonic movements without significant side-effects.

The neurologic mechanism of myoclonus is unclear, although it may be a form of seizure activity. Researchers have suggested that it is a disinhibition phenomenon, because large doses of etomidate depress cortical activity before they depress subcortical activity [12, 14, 15]. Pretreatment with benzodiazepines and opioids, drugs known to inhibit subcortical neuronal activity, abolish myoclonus [15]. Also, in recent research Choi et al. [16] showed that pretreatment with rocuronium significantly reduced the frequency of myoclonus due to etomidate by blocking transmission at the neuromuscular junction. But clinically distressing side effects are frequently observed, for example sedation, apnea, chest muscle rigidity, cardiovascular depression for opioids, delayed recovery for benzodiazepines, and airway obstruction, regurgitation, and aspiration for muscle relaxants [10, 13, 16]. An ideal pretreatment drug for preventing myoclonic movements should be short-acting, not have significant effects on respiration and hemodynamics, and not prolong recovery from anesthesia [10]. In this respect, pretreatment of myoclonus with lidocaine is capable of reducing the occurrence of myoclonic movements and deserves further study.



$^{*}p < 0.01$; compared to group S

Fig. 1 Assessment of myoclonus. $^{*}p < 0.01$; compared with group S

We should also note that the inhibitory effect of lidocaine on etomidate-induced myoclonus was weaker than that of midazolam or some narcotics. Whether higher doses of lidocaine can exert a stronger inhibitory effect without adverse effects is to be tested by future studies.

Lidocaine pretreatment may modify vascular pain on etomidate injection because of its local analgesic effect of stabilizing the kinin cascade [17]. But how lidocaine works in suppressing etomidate-induced myoclonus is not clear. It may be speculated that pretreatment with lidocaine may reduce the excitability of the CNS which is the cause of myoclonic movements [3].

In conclusion, this study showed that pretreatment with lidocaine before induction with etomidate significantly reduced the frequency and severity of myoclonus.

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