Case Report

Grand mal seizure induced by low-dose fentanyl and lidocaine in a young child

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ABSTRACT

Surgical procedures require general anesthesia using combinations of drugs including fentanyl and/or lidocaine. Because many of these drugs have bimodal anticonvulsant/proconvulsant effects, they must be administered carefully. We herein report a case of seizure attack during anesthesia induction with low-dose fentanyl and lidocaine in a young child with no history of seizures. A 10-year-old girl was scheduled to receive an elective tenectomy. After a few seconds of fentanyl and lidocaine administration for anesthesia induction, she developed generalized tonic-clonic seizures. Seizures subsided spontaneously after 3 minutes. The patient’s blood sugar, serum electrolytes, and arterial blood gas analysis were normal immediately after the event. She remained hemodynamically stable; however, the surgery was postponed after communication and discussion with the surgeon. Postoperatively, there was no evidence of postictal phase, and serum electrolytes and magnetic resonance imaging of the brain were normal. The patient had an uneventful recovery. However, electroencephalogram showed that hyperventilation stimulation test induced isolated epileptiform spikes over O1, suggesting a potential paroxysmal disorder over the left occipital area. This report is on a rare complication likely caused by fentanyl or lidocaine, which suggests that these drugs should be used cautiously in children whose clinical epileptic activities have been verified or are strongly suspected.

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1. Introduction

Seizures are episodes of abnormally synchronized electrical brain activity. It is estimated that 2% of the general population will experience a seizure during their lifetime. Benign childhood focal seizures affect 20–25% of children with nonepileptic seizures. The typical onset is between 1 year and 12 years, with peak incidence at 5 years, and remission within 1–2 years from onset. In one third of the patients, seizures (or even partial status epilepticus) are single events in the child’s life. The mean number of seizures is three and the maximum is 15. The new classification system of the International League Against Epilepsy Task Force identified three types of benign childhood focal seizures, namely, benign childhood epilepsy with centrotemporal spikes, early onset benign childhood occipital epilepsy (BCOE; Panayiotopoulos type), and late-onset childhood occipital epilepsy (Gastaut type). Although early onset BCOE is identified by occipital spikes on the electroencephalogram (EEG), they may also occur in children who do not suffer from seizures and in those with severe symptomatic epilepsies.

Several anesthetic and analgesic drugs may have both anticonvulsant and proconvulsant effects. For example, lidocaine at 0.5–5 μg/mL serum concentration is used to treat epileptic episodes, whereas higher doses are proconvulsant. In most cases, adult patients experience a brief general tonic-clonic (grand mal) seizure postoperatively. However, they occasionally develop grand mal seizures within seconds of anesthesia administration. A few adult patients have had a brief episode of grand mal seizure after receiving low-dose fentanyl. Two adults with a history of epilepsy suffered a grand mal seizure after low-dose lidocaine administration.
Recently, a 4-month-old infant undergoing elective circumci-
sion developed tonic–clonic convulsions after the administration of
lidocaine.14 This case study suggested that infants and children are
also susceptible to intraoperative anesthesia-induced seizures. Here,
we report the case of a 10-year-old child, with no history of
seizures, who required surgery for tenectomy due to wry neck
torticollis). The administration of low-dose fentanyl and lidocaine
was followed by a brief episode of grand mal seizure. This report
suggests that fentanyl or lidocaine should be used cautiously in
children especially in those whose clinical epileptic activities have
been verified or are strongly suspected.

2. Case Report

A 10-year-old girl (height, 146 cm; weight, 54 kg) was sched-
uled for an elective tenectomy of the left sternocleidomastoid
muscle due to torticollis. She was robust and had no febrile
convulsion or previous noteworthy medical history. She was pre-
viously never administered even dental anesthesia. In addition,
she had no medical history of cardiovascular complications such as
intracerebral abscess, neurological complications (epilepsy), or
infections (viral encephalitis) that could predispose her to a
seizure. At the time of admission, the laboratory data and physical
examination showed no abnormalities (glucose, 105 mg/dL; blood
urea nitrogen, 10 mg/dL; creatinine, 0.4 mg/dL; aspartate amino-
transferase, 28 U/L; alanine transaminase, 25 U/L; Na⁺, 142 mmol/
L; K⁺, 4.1 mmol/L; Cl⁻, 108 mmol/L; white blood cells, 7800/μL;
hemoglobin b, 12.6 g/dL; platelet count, 169,000/μL; and pro-
thrombin time/partial thromboplastin time/international normal-
ized ratio, 9.7 s/26.2 s/0.9). She came to the operating room
without any premedication. Blood pressure was 115/82 mmHg and
heart rate was 75 beats/min. Under mask inhalation of 100% ox-
ygen, 100 μg (1.85 μg/kg) of fentanyl was slowly administered
intravenously in 30 seconds; 50 mg (0.93 mg/kg) of lidocaine was
also administered intravenously in 3 seconds. Immediately after
the administration of the lidocaine dose, the patient experienced
general muscle contraction and rigidity, which were more prom-
inent over the trunk and the upper and lower extremities. In
addition, she had violent rhythmic muscle contraction and relax-
ation, and we also noted that she bit her tongue, clenched her
mouth was initiated. After 3 minutes, the patient regained
consciousness spontaneously, but the surgery was postponed.

She lost consciousness and did not respond to verbal commands
soon after. Because the seizure activity was interfering with her
breathing, bag–valve–mask (BMV) ventilation through the nose
and mouth was initiated. After 3 minutes, the patient regained
consciousness spontaneously, but the surgery was postponed.

On Day 1 following the seizure episode, the patient was tested
for congenital heart disease or structural brain lesions by echo-
cardiography, magnetic resonance imaging (MRI) of the brain, and
EEG during hyperventilation stimulation testing. The echocardi-
ogram and brain MRI results were normal. However, hyperventila-
tion stimulation induced isolated spikes over O1 on the EEG,
This finding and the short duration of the preoperative seizure, the patient was diag-
nosed with late-onset childhood occipital epilepsy (Gastaut type).

Because the surgery was postponed, we transferred the patient
to the pediatric intensive care unit for further observation and
management. Fortunately, the patient was transferred to the gen-
eral ward in 1 day as her condition stabilized and was discharged 2
days later without any neurological sequelae.

Owing to the anesthesia-induced seizure, we discussed
providing conservative treatment for wry neck with her parents,
for which they agreed.

Written informed consent and informed assent were obtained
from the parents and the patient, respectively.

3. Discussion

Surgical procedures commonly require general anesthesia using
combinations of drugs including fentanyl and/or lidocaine. Because
many of these drugs have bimodal anticonvulsant/proconvulsant
effects, dosage guidelines are carefully designed for the safety of the
patients.5 Herein, we reported the case of a 10-year-old child
who suffered a grand mal seizure within seconds of receiving
intravenous fentanyl (1.85 μg/kg) and lidocaine (0.93 mg/kg). The
patient recovered spontaneously after 3 minutes. This adverse ef-
fect was not anticipated, because the patient had no medical his-
tory of spontaneous or anesthesia-related seizures. Based on the
patient’s age, the normal echocardiogram and MRI findings, but
abnormal EEG finding during hyperventilation testing, the patient
was diagnosed with late-onset childhood occipital epilepsy (Gas-
taut type).

Anesthesia-induced seizures have been reported with these
drugs in adults13–17 and in an infant.18 Grand mal seizure was
also reported in an adult who received fentanyl (2.53 μg/kg).10
Narcotic seizures were more likely to originate in the subcor-
tical nuclei. Therefore, fentanyl may produce seizure activity in
the subcortical areas, which would not be detectable by surface
electrodes.18 However, hyperventilation stimulation induced
isolated epileptiform spikes over the O1 area on the EEG. This
suggested that the grand mal seizure in this case might be less
related to fentanyl administration. Serum concentrations of
lidocaine exceeding 5 μg/mL have been reported to lower the
seizure threshold in the cerebral cortex, amygdala, hippocam-
pus, and thus cause a generalized seizure.11 DeToledo et al15
reported that continuous intravenous infusions of lidocaine to
11 healthy volunteers at rates ranging from 1.5 mg/kg/min to
3 mg/kg/min resulted in generalized convulsions in all after an
average total dose of 6–8 mg/kg. Modica et al17 reported that a
lidocaine dose of 16.5 mg/kg produced tonic–clonic seizure in
50% of patients. By contrast, in children receiving continuous
infusions of lidocaine, adverse effects have been reported at
levels of 1.8–4.7 μg/mL.19 From these reports, we can deduce
that the dosage of lidocaine proconvulsant is lower in children
than in adults. Just after the seizure episode, the patient was
tested for congenital heart disease or structural brain lesions by
echocardiography, MRI of the brain, and EEG during hyperven-
tilation stimulation testing. Seneviratne et al10 reported that
hyperventilation action activating test may increase the rate of
generalized discharges in children without epilepsy or other
generalized epilepsies. The EEG results indicated that the
occurrence of grand mal seizure behavior in this child was due
to brain epileptogenic discharge. It was also deduced that the
brain discharge was mainly caused after the administration of
fentanyl and lidocaine. In theory, the lidocaine dose (0.93 mg/
kg) administered was low and in itself should not induce
convulsion. However, it is probable that the grand mal seizure
may have occurred following the combined use of fentanyl with
lidocaine in this case. These findings suggest that the serum
toxic levels of fentanyl and lidocaine in children are different
from those in adults, and that careful observation and man-
agement for children on lidocaine therapy is necessary, despite
the range of serum lidocaine levels being within the therapeutic
level. We also summarized the results of published papers on
fentanyl or lidocaine-induced seizure in Table 1.

Drug interactions have also been reported between lidocaine
and fentanyl.21 Chergn and Wong22 have demonstrated that fen-
tanyl potentiates the lidocaine-induced convulsions in a dose-
dependent manner in mice, and the effect may be mediated by an opioid mechanism. This study suggests that low-dose fentanyl may lower the threshold of lidocaine-induced seizure, especially in patients with characteristics of easy-provoked epileptiform discharge, as shown by the EEG in this child who received a low-dose fentanyl and lidocaine.

We also performed an echocardiography to detect whether the patient had any congenital heart disease, such as patent foramen ovale, ventricular septal defect, or atrial septal defect as even a small dose of fentanyl or lidocaine can induce seizure in these patients.23

The management of anesthesia-induced seizures involves immediate deepening of anesthesia, administration of an anticonvulsant agent, and subsequent correction of any reversible precipitating factor.1 In our case, treatment was not necessary, because after the BMV ventilation through her nose and mouth, the seizure subsided spontaneously and her vital signs stabilized. Based on these observations, we did not prescribe any anticonvulsant agent.

Our case report emphasizes five key points: (1) the serum toxic levels of fentanyl and lidocaine in children are different from those in adults. (2) Combination of fentanyl and lidocaine should be used very cautiously for potential cases in which epileptic activities are easy triggered. (3) Cardiogenic factors, such as congenital heart disease, should be kept in mind if seizure attack happened in the operation room without any obvious cause. (4) Although lidocaine lowers the occurrence of cough, laryngeal spasm, and arrhythmia when performing general anesthesia, it may not be routinely used in children. (5) One of the causes of acquired wry neck might be neurologic disorders in the central nervous system,24 which could lower the threshold of seizure, and therefore, we should use fentanyl and lidocaine more carefully in these patients.

Acknowledgments

Thanks to all staff in the Tri-Service General Hospital, Taipei, Taiwan and Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan.

Table 1
Summary of literatures about fentanyl or lidocaine-induced seizure.

<table>
<thead>
<tr>
<th>Author</th>
<th>Fentanyl-induced seizure</th>
<th>Lidocaine-induced seizure</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safwat and Daniel10</td>
<td>+</td>
<td>−</td>
<td>79 y/o, 79 kg Fentanyl 200 µg</td>
</tr>
<tr>
<td>Hoien et al11</td>
<td>+</td>
<td>−</td>
<td>17 y/o Fentanyl 100 µg</td>
</tr>
<tr>
<td>Fujimoto et al12</td>
<td>+</td>
<td>−</td>
<td>79 y/o, 54 kg Fentanyl 100 µg</td>
</tr>
<tr>
<td>DeToledo et al13</td>
<td>−</td>
<td>+</td>
<td>36 y/o, Lidocaine serum concentration: 21 µg/mL Case 1 36 y/o, Lidocaine 100 mg</td>
</tr>
<tr>
<td>Ozer AB et al14</td>
<td>−</td>
<td>+</td>
<td>4-month-old 8.9 kg Lidocaine 100 mg</td>
</tr>
<tr>
<td>Moran LR et al16</td>
<td>−</td>
<td>+</td>
<td>25-day-old 2.514 kg Lidocaine serum concentration: 0.7 µg/mL</td>
</tr>
<tr>
<td>Sata Y et al19</td>
<td>−</td>
<td>+</td>
<td>Lidocaine serum concentration: 1.8–4.7 µg/mL in children</td>
</tr>
<tr>
<td>Baraka A et al21</td>
<td>+</td>
<td>+</td>
<td>24 y/o, 60 kg Fentanyl 600 µg Lidocaine 120 mg</td>
</tr>
</tbody>
</table>

Fig 1. Electroencephalogram report: hyperventilation stimulation test induced isolated spikes over O1 (black arrow), suggesting a paroxysmal disorder over the left occipital area.
References