·临床经验·

Detection of seizures with amplitude-integrated electroencephalography in a neonate treated with extracorporeal membrane oxygenation

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Abstract: Infants with severe cardiorespiratory failure treated with extracorporeal membrane oxygenation are at risk of hypoxic-ischemic injury and infarction of the brain, intracranial hemorrhage, and seizures. Consequently, this can lead to adverse neurodevelopmental outcome. We present a neonate treated with veno-arterial extracorporeal membrane oxygenation due to diaphragmatic hernia. The infant's brain function was continuously monitored with amplitude-integrated electroencephalography. The child experienced clinical seizures and subclinical seizure discharges, detected by amplitude-integrated electroencephalography, permitting the opportunity to treat them and adjust the anticonvulsive treatment accordingly. [**Chin J Contemp Pediatr**, **2008**, **10** (**4**):**547 – 551**]

Key words: Amplitude-integrated electroencephalography; Cardiorespiratory failure; Extracorporeal membrane oxygenation; Seizure; Neonate

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Introduction

Extracorporeal membrane oxygenation (ECMO) is used to treat infants with severe cardiorespiratory failure. Despite ECMO being a life-saving therapy, the morbidity of patients receiving ECMO treatment is primarily related to neurological alterations. The infants treated with ECMO are at risk of hypoxic-ischemic injury and infarction of the brain, intracranial hemorrhage, seizures, and consequently adverse neurodevelopmental outcome[1]. Some studies have found that the evaluation of infants during ECMO with standard electroencephalography (EEG) is of predictive value regarding neurodevelopmental outcome. In a study of Streletz et al [2], death or developmental disability occurred in 7 of 11 infants treated with ECMO who presented electrographic seizures on standard EEG, while it occurred in only 31 of 100 infants without electrographic seizures. Graziani et al [3] reported that serial standard EEG recordings, in comparison to a single standard EEG recording, increased the predictive value of EEG in infants.

While standard EEG recording is usually of 20-30 minutes duration, amplitude-integrated EEG (aEEG) enables continuous monitoring of brain function over several hours or even days. Monitoring with aEEG has been used extensively in newborns with hypoxic-ischemic encephalopathy (HIE). The aEEG has been used for assessment of background pattern, detection of seizures, evaluation of the effects of anticonvulsive drugs, and prediction of neurodevelopmental outcome[4,5]. In a study by Pappas et al[6] on 20 newborn infants treated with ECMO, an abnormal aEEG predicted death or moderate to severe intracranial neuropathology. With the encouraging results of studies evaluating the neuroprotective effects of induced hypothermia, this treatment has also been applied to patients treated with ECMO. Mild hypothermia does not influence the aEEG tracings, suggesting that cerebral monitoring with aEEG is possible during mild hypothermia[7,8].

In studies comparing aEEG and standard EEG, the background patterns in the sick full-term infant seem to correlate well[9]. Although standard EEG remains the

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gold standard for detection and quantification of neonatal seizures, continuous monitoring of brain function with aEEG is an important supplemental diagnostic method[10].

We present a newborn treated with veno-arterial ECMO, whose brain function was continuously monitored with aEEG. Although we performed standard EEG in this patient, additional monitoring with aEEG gave us the opportunity to better respond to clinical and subclinical seizures experienced by the patient.

Case study

The patient was an infant girl, born at 38 weeks' gestation to a 28-year-old mother in a regional maternity hospital. The mother became pregnant while undergoing *in vitro* fertilization treatment. The mother's medical history was unremarkable and the pregnancy uneventful. The infant girl was born by vaginal delivery in a vertex position, 6.5 hours after spontaneous rupture of membranes. The infant cried at first, then suddenly ceased breathing, became cyanotic and bradycardic. The Apgar scores were 8, 3, and 3 at 1, 5, and 10 minutes, respectively. Cardio-pulmonary resuscitation was initiated; the infant was then intubated and artificially ventilated. Left-sided pneumothorax was present and a chest drain was placed. The transcutaneously measured arterial saturation remained below 80% in spite of oxygen supplementation, and the infant was subsequently transferred to the Level III Multidisciplinary Neonatal and Pediatric Intensive Care Unit of the University Medical Center Ljubljana, Slovenia. Nitric-oxide therapy was initiated and high frequency ventilation started. Diaphragmatic hernia was seen on X-ray and echocardiography revealed poor contractility of the left ventricle. The infant underwent a repair operation, but following surgery she became hemodynamically unstable and eventually ECMO was initiated 35 hours after birth. Brain ultrasound on day 3 of ECMO treatment revealed diffuse increase in echogenicity of the brain tissue, without signs of intracranial hemorrhage. The aEEG tracings recorded with the cerebral function monitor (CFM 4640, Lectromed Devices Ltd, Hertfordshire, UK) are shown in Figure 1. Before the initiation of ECMO, the background pattern deteriorated from slightly discontinuous to severely discontinuous burst-suppression pattern. Within the first 1 hour of ECMO, the background pattern improved to continuous normal voltage pattern. After 3 days of ECMO treatment, the background pattern again became slightly discontinuous. Subclinical seizure discharges were present on the aEEG tracing, as well as a single seizure

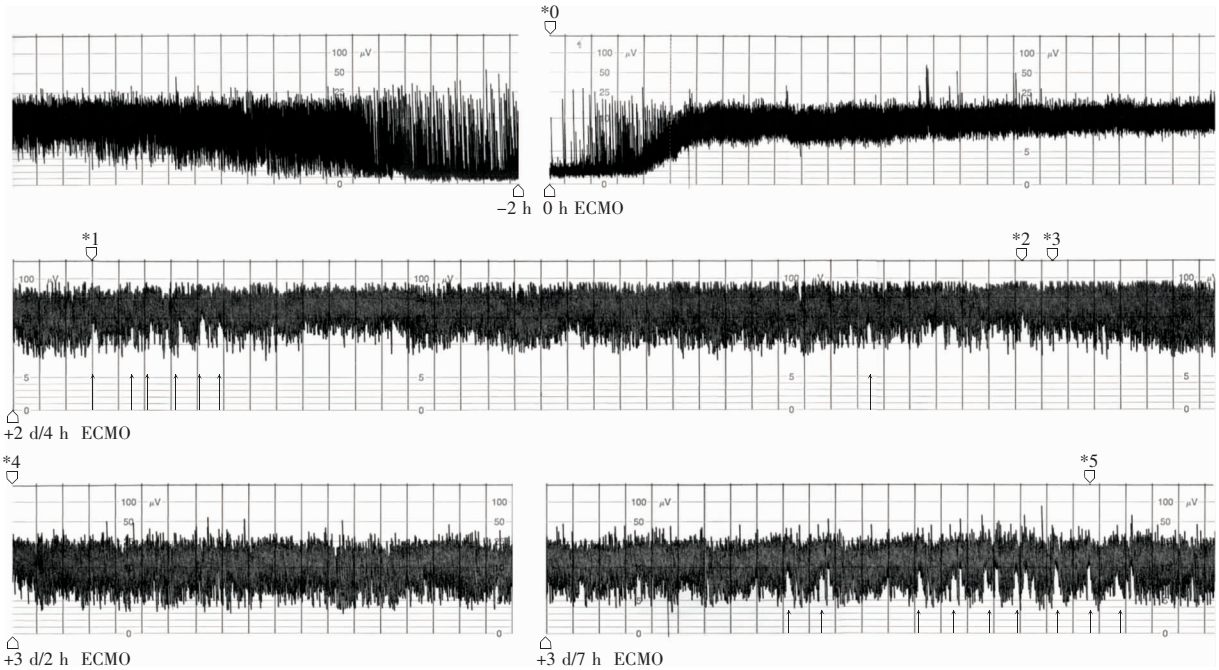

Figure 1 The aEEG tracings of the infant *0, start of ECMO; *1, clinically silent repetitive seizure discharges; *2, a single clinical seizure; *3, introduction of phenobarbital treatment; *4, time point at which standard EEG was performed; *5, introduction of thiopental treatment after presentation of clinically silent repetitive seizure discharges on aEEG tracing; arrows mark the clinically silent seizure discharges.

discharge that was accompanied by signs of a clinical seizure. Phenobarbital treatment was started (20 mg/kg/dose, twice a day), but clinically silent seizure discharges reappeared. Treatment with thiopental was started (2 mg/kg/dose, repeated as needed) and no seizure discharges were seen on the aEEG tracing afterwards. No sleep-wake cycling was present on the aEEG tracing throughout the recording.

Standard EEG performed 74 hours after initiation of ECMO showed discontinuous background pattern and multifocal presence of sharp waves, without overt hypersynchronous seizure discharges (Figure 2).

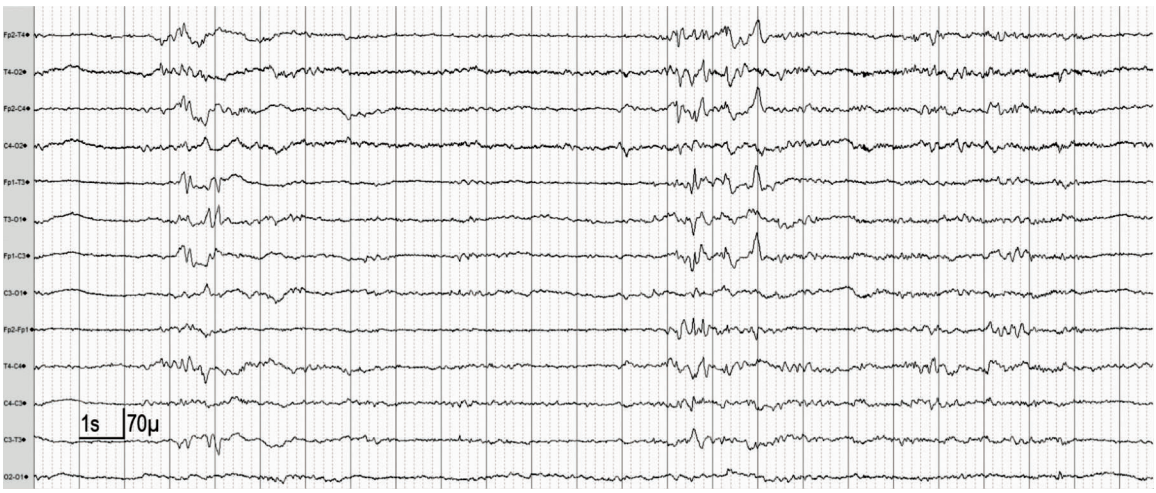

Figure 2 The most pathological part of the standard EEG as recorded at the time point ＊4 of Figure 1.

During the 6 days of ECMO treatment, the infant did not show any signs of cardiocirculatory and respiratory improvement and she remained fully dependent on maximum ECMO blood flow of 300 mL/kg/minutes. The treatment was eventually discontinued on day 8 of life, which led to the infant's death. The autopsy revealed hemorrhage in the left cerebellar hemisphere, hypertrophy of the right ventricle, hypoplasia of the left lung, and other changes concordant with the diagnosis of diaphragmatic hernia.

Discussion

This case demonstrates the possible benefits of continuous cerebral function monitoring with aEEG in newborns treated with ECMO. These newborns are at risk of having seizures, which are associated with adverse neurodevelopmental outcome[5]. Treatment with ECMO often requires sedation and paralysis of the newborns, as was the case in this study. This renders the detection of seizures by clinical signs unreliable. The standard EEG recording is usually of only 20 minutes duration; therefore, the seizure discharges can easily be missed. In this patient, the standard EEG showed sharp waves, but no overt seizure discharges that would urge the immediate introduction of an anticonvulsive drug. However, this patient did experience both a clinical seizure and clinically silent seizure discharges. The first-line anticonvulsive treatment failed to the first clinical seizure and subsequent clinically silent seizure discharges were detected with aEEG, which gave the opportunity to modify anticonvulsive treatment appropriately. Newer digital aEEG monitors provide the option of simultaneous presentation of aEEG signal and the raw EEG signal, which might give additional information when the presence/absence of seizures is uncertain.

The initiation of ECMO treatment rapidly improved the aEEG background pattern. Before ECMO, severely abnormal burst-suppression background pattern was present on aEEG tracing, caused by the underlying disease process. The discontinuous background pattern normalized to a continuous normal voltage pattern within 1 hour of ECMO treatment. This is in accordance with the findings of Pappas et al[6], who have found an improvement in aEEG background pattern within 24 ± 8 hours of ECMO treatment.

No sleep-wake cycling was seen on aEEG tracings in

this patient. Although conclusions cannot be drawn from a single case, it is not uncommon that the infants with hypoxic-ischemic brain injury fail to present a sleep-wake cycling on aEEG or present it with a significant delay[11].

The right common carotid artery is usually employed for bypass in ECMO patients, as was the case in this study. Some studies have shown a predilection for right hemispheric structural and functional abnormalities in ECMO-treated neonates, while others have not reported consistent laterality. If lateralized abnormalities are suspected, 2-channel aEEG might provide additional data when monitoring newborns treated with ECMO.

Monitoring of cerebral function in newborns treated with ECMO is important from the diagnostic, therapeutic, and prognostic perspectives. This case demonstrates that continuous monitoring of brain function with aEEG can provide additional data, which can be used to better treat these children. Additional studies are needed to further elucidate the value of aEEG in newborns treated with ECMO.

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(译文附后)

·译文·

应用振幅整合脑电图监测体外膜肺治疗过程中的新生儿癫癎 1 例(摘译)

李萌　译,杨于嘉　校

体外膜肺(ECMO)通常用于挽救对呼吸机治疗无效的新生儿的生命,但经体外膜肺治疗的患儿易发生缺氧缺血性损伤、脑梗塞、颅内出血和癫癎发作,因此对神经发育造成不良影响。

用标准脑电图(EEG)描记评估体外膜肺治疗新生儿的神经发育结果具有预测意义,连续的标准 EEG 记录可提高预测价值。标准 EEG 通常连续记录时间为 20 ~ 30 分钟,而振幅整合脑电图(aEEG)可超过几小时甚至几天。aEEG 已广泛应用于缺氧缺血性脑病患儿的诊断,癫癎发作的监测,解痉药的疗效评价以及神经发育的预测。目前 aEEG 用于 ECMO 治疗新生儿的脑功能监测很少有报道。该文报道 1 例新生儿用 aEEG 连续监测 ECMO 治疗过程中的脑功能变化。

患儿女,胎龄 38 周,于破膜后 6.5 h 头位顺产。母 28 岁,试管内受精怀孕。新生儿出生时有哭声,之后突然呼吸停止。Apgar 评分 1 min 8 分,5 min 3 分,10 min 3 分。予以心肺复苏,气管插管。出现左侧气胸,放置胸腔引流。给予氧气吸入后经皮动脉血氧饱和度仍低于 80%。患儿被转入斯洛文尼亚 Ljubljana 大学医学中心的 III 级综合儿科和新生儿 ICU,给予一氧化氮和高频通气治疗。X 射线示膈疝,超声心动图示左心室收缩减弱,行膈疝修复手术。术中出现血流动力学的不稳定,最终在其出生 35 h 后予以 ECMO 治疗。ECMO 治疗的第 3 天脑超声显示脑组织回声弥散性增强,无颅内出血的征象。

aEEG 记录仪(CFM 4640, Lectromed Devices Ltd, Hertfordshire, UK)记录的患儿脑电波形变化见图 1。在 ECMO 治疗开始时,aEEG 背景波出现轻度中断至严重中断的爆发性抑制,1 h 后背景波恢复为连续的电压正常的背景波,ECMO 治疗 3 天后再次出现轻度不连续的背景波。无论是亚临床型发作还是有临床症状的发作均在 aEEG 中记录到癫癎样放电。予以苯巴比妥治疗后(20 mg/kg,1 日 2 次),亚临床型发作时仍可在 aEEG 描记中出现癫癎样放电。然而当给予硫喷妥钠治疗后(2 mg/kg,按需重复),aEEG 描记未再出现癫癎样放电,提示亚临床型发作消失。aEEG 描记自始至终未出现睡眠-觉醒周期(SWC)。在 ECMO 治疗 74 h 后,标准 EEG 虽也可显示不连续的背景波和多灶性尖波,但无明显高度同步的癫癎样放电(图 2)。在 ECMO 治疗的 6 天中,患儿循环和呼吸未出现任何改善的征象,需完全依赖最大血流量为每分钟为 300 mL/kg 的 ECMO 治疗。最终于生后第 8 天停止治疗,患儿死亡。尸检显示左侧小脑半球出血,右侧脑室扩大,左肺发育不全以及膈疝。

新生儿在 ECMO 治疗过程中,由于缺氧缺血影响可能有抽搐的发作,从而影响神经发育。使用 ECMO 治疗时,病人经常需要使用镇静剂和阿片类的止痛剂,此时依靠临床症状来判断抽搐的发作是不可靠的。标准 EEG 一般只记录 20 分钟,因此抽搐发作时的放电不容易被捕获。本病例在标准 EEG 上虽显示有尖波,但没有发现需要紧急使用止惊药的典型癫癎样放电。而事实上该病人确实有典型的和隐匿型的癫癎发作。她在首次临床发作后使用了一线的抗惊厥药治疗失败,随后的隐匿型发作被 aEEG 检测到,从而使病人获得了调整抗惊厥药的机会。右颈总动脉是 ECMO 治疗病人常用的通路,因此在 ECMO 治疗的新生儿中易造成右侧大脑半球结构和功能的异常。2 导联 aEEG 的监测可为 ECMO 治疗中的新生儿提供一侧大脑功能异常的证据。此病例表明,使用 aEEG 连续监测 ECMO 治疗下的新生儿大脑功能是重要的,它有助于反映治疗过程中脑功能的变化和不典型癫癎发作的诊断。