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LETTER TO THE EDITOR

Possible effect of perampanel on focal status epilepticus after generalized tonic–clonic status epilepticus

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Introduction

Since in refractory status epilepticus (SE), additional glutamate receptors such as alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) and *N*-methyl-D-aspartate (NMDA) receptors are built up in the synaptic membrane [1], perampanel, a novel noncompetitive AMPA-receptor antagonist, may be effective in this condition. During the treatment of refractory SE, usually a combination therapy of several antiepileptic drugs (AEDs) is established. Therefore, the drug, which has terminated the SE, cannot easily be identified. A possible effect of an AED on the termination of a SE may be supposed, when the termination of a SE is associated with the introduction of an AED in the therapy or an increased dose of an AED in combination with other changes in the antiepileptic medication at the same time [2]. Here we present a case where perampanel was the last AED introduced in the treatment of a focal SE before its termination 24 h later.

Case report

A women aged 81 years with symptomatic epilepsy following a stroke 2 years before was found with generalized tonic–clonic SE in her nursing home. Her regular medication was levetiracetam 500 mg and valproate 1,800 mg. This SE was terminated with 2 mg clonazepam i.v. by the emergency doctor. But myoclonic jerks of the left arm and the left side of the face persisted. ICU admission was clearly forbidden by directives from the patient's power of attorney. After cumulative doses of levetiracetam 2,750 mg, valproate 600 mg, lorazepam 1.5 mg, acetazolamide 250 mg and lacosamide 100 mg, perampanel 2 mg was introduced into the therapy with little success. The electroencephalogram at this time showed repetitive series of spikes, which were associated with myoclonic jerks (see Fig. 1). Another 1 mg clonazepam and 1,000 mg levetiracetam were given on the same day to terminate the jerks for a few hours. The treatment regime scheduled for the next day was levetiracetam 4,000 mg, valproate 1,800 mg, lacosamide 200 mg. Additionally another 2 mg perampanel was given in the morning. In the afternoon another 1 mg clonazepam was needed to suppress the jerks. Afterwards another 2 mg perampanel was given and the daily dose of perampanel was increased to 2 mg twice a day. After this, no further spontaneous myoclonic jerks were seen. The further course was complicated by haemorrhagia in the thigh after which anticoagulation (that the patient had received for atrial flutter) was stopped. The patient was transferred to the department of internal medicine. At this time, the valproate total serum level was 37.2 mg/l. Due to a low albumin serum level, the free valproate serum level was 9.99, which is in the upper therapeutic range. During the treatment of acute anemia in the department of internal medicine, perampanel was accidently stopped and due to the administration of meropenem for the treatment of pneumonia, the valproate serum level was reduced to 9 mg/l and myoclonic jerks reoccurred. After 2 days, perampanel was reestablished and increased to 6 mg/day. Valproate was given intravenously to increase the bioavailability. Myoclonic jerks stopped again. Lacosamide was reduced and finally stopped within 9 days and levetiracetam reduced to 3,000 mg/day without any recurrence of myoclonic jerks. Finally, the patient was discharged with a treatment regime of levetiracetam 3,000 mg/day, valproate

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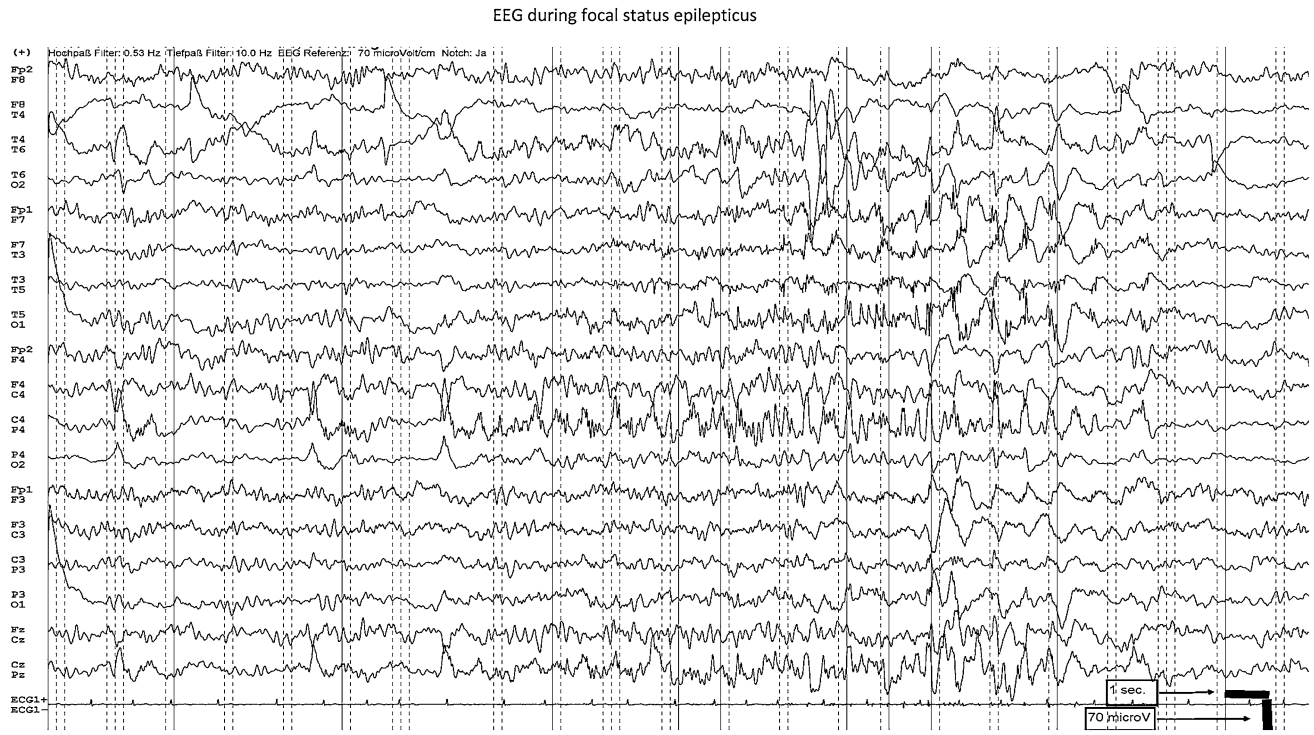

Fig. 1 EEG during focal status epilepticus. Note the train of spikes in channels 10 and 11, which is followed by muscle artifact in the left temporal channels (e.g., 5–8)

1,800 mg/day and perampanel 6 mg/day to her nursing home in the same clinical condition, in which she had been before the SE. On discharge, her free valproate serum level was 5.67 mg/l, which is in the lower therapeutic range. Her perampanel serum level was 408 ng/ml. The therapeutic range for perampanel is not established yet.

Discussion

Treatment of nonconvulsive SE in critically ill elderly patients still is an unsolved problem. In fact, patients who are treated outside ICU according to an advance directive may have a shorter hospital stay than patients treated in ICU [3]. So there is a need of AEDs which may terminate refractory nonconvulsive status epilepticus without requiring ICU treatment. In our patient, perampanel was the last AED introduced in therapy before the termination of EPC. Since the starting dose was very low, EPC did not stop immediately after the first administration. After increasing the dose of perampanel and the other established AEDs EPC was terminated. It recurred when perampanel was accidently stopped and valproate serum level was lowered. With an increase of the dose of perampanel and the administration of valproate intravenously to improve bioavailability, EPC was terminated again. Therefore, according to the proposition of Stojanova and Rossetti [2] besides the effect of the other AEDs used in our patient, perampanel might have had an effect on refractory SE. The low dose of valproate was chosen because valproate was already established in the medication. Therefore, no loading dose was needed. The patient weighted only 50 kg. Therefore, we administered very low doses. Especially lacosamide was given very carefully because we experienced a transient third-degree atrioventricular block after a faster titration in another elderly patient [4].

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Conflict of interest Prof. Dr. R. Benecke received speaker honorium from GlaxoSmithKline, Dr. Chr. Kampf has no conflict of Interest, Dr. J. Rösche received speaker honoraria from GlaxoSmithKline and EISAI, travel grants form UCB GmbH and was medical advisor for EISAI.

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