

## CASE REPORT

# Case reports of covert use of phenobarbital in patients taking Diankexing and Diankening, traditional herbal medicine for epilepsy

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### Abstract

This is a report of three patients with drug resistant epilepsy, who was prescribed Diankexing and Diankening, herbal medicine for treatment of epilepsy by the traditional Chinese medicine physicians. Analysis of the medications from all the 3 patients showed Diankexing to contain phenobarbital, and Diankening from one patient. One patient had overt phenobarbital toxicity, and two others had phenobarbital side effects. Physicians should be aware of possible adulterations with conventional antiepileptic drugs in patients purported taking traditional medicine, with potential adverse effects and drug interactions.

### INTRODUCTION

The use of traditional herbal medicine for treatment of epilepsy is common in Asia especially among the ethnic Chinese population in the region. In a study conducted in the Veteran General Hospital, Taipei, traditional Chinese medicines were used in combination with conventional antiepileptic drugs in 16.32 per cent of 729 patients with epilepsy.<sup>1</sup> The use of traditional herbal medicine can incur significant economic burden to the patients. A study conducted in Veterans General Hospital, Kaoshiung, Taiwan reported 11 newly diagnosed patients with epilepsy spending an average of 60 to 100 USD monthly on traditional Chinese medicine. There has also been report of covert use of Western antiepileptic drug in supposed traditional Chinese medicine. In the Kaoshiung study, 5 of the patients who were still taking the medicine showed elevated serum phenytoin level from 3.79-41.06 mg/ml, and phenobarbital level from 2.76-23.37 mg/ml. An analysis of the Chinese medicine from one of the patients was positive for phenytoin and phenobarbital.<sup>2</sup> Diankexing 癩克星 and Diankening 癩克寧 are two traditional herbal medicine commonly prescribed to patients with epilepsy by traditional Chinese physicians in Malaysia. The drugs sold in Malaysia were purported to be manufactured in various cities in China, with some being packaged in Malaysia. We report three patients with epilepsy at the Neurology

Unit, University of Malaya Medical Centre, Kuala Lumpur, who has covert use of phenobarbital with taking Diankexing and Diankening.

### CASE REPORT 1

This 38 year old woman of ethnic Chinese origin was a housewife. She had been diagnosed to have cryptogenic complex partial seizure since 5 years old. She had absence and generalized convulsive seizures. Other than seizures, there was no other medical history of note. Physical examination was also normal. Electroencephalography showed discharges from both temporal areas. MR imaging was normal. Her current antiepileptic drugs were carbamazepine, sodium valproate and topiramate. She has previously been on phenytoin, lamotrigine, and gabapentin. Despite the medications, she continued to have frequent seizures averaging 2-3 times a month.

About 3 months before the recent illness, she also took Diankexing and Diankening in addition to the antiepileptic medications prescribed by the hospital. This was on the advice from her traditional medicine physician. There was improvement in the seizure control. However, she also felt increased drowsiness and slurred speech. As such, she reduced on her own by half, the dosage of carbamazepine, sodium valproate and topiramate. She was admitted to hospital with exacerbation of seizures, 12 seizures over two days. On admission she was drowsy but

oriented. Her speech was slurred and scanning. There was nystagmus in all directions of gaze, truncal and limb ataxia. EEG showed intermittent diffuse irregular slow waves with bitemporal independent sharp waves. Serum anticonvulsant levels showed carbamazepine of < 0.10 mg/dL (normal 4.0 to 10.0), valproate of < 3.2 mg/dL (normal 40 to 100), phenytoin of 0.7 mg/dL (normal 10.0 to 20.0), and phenobarbital of 60 mg/dL (normal 20.0 to 40.0). She improved after discontinuing Diankexing and Diankening. Subsequent analysis revealed the presence of phenobarbital in Diankexing. No known anticonvulsants were detected in Diankening.

## CASE REPORT 2

This 37 year old woman of ethnic Chinese origin has epilepsy since age 11 years. The seizure consisted drop attack and generalized convulsions. Other than seizures, there was no other medical history of note. Physical examination was also normal. Electroencephalography showed left temporal discharges. MR imaging did not show any definite focal lesion. Her current medications consisted of sodium valproate, carbamazepine, lamotrigine, and clonazepam. She has previously also taken phenobarbital, phenytoin, levetiracetam and nitrazepam. Despite these medications, she continued to have 2 to 3 seizures a month. The patient also admitted to taking Diankexing and Diankening in addition to the anticonvulsants prescribed by the Hospital for the previous 4 years. When she first started the medications, there was seizure freedom for about six months. However, she also had excessive drowsiness, double vision and ataxia. These symptoms improved when she reduced the doses of the drugs, though mild ataxia persisted. Serum anticonvulsant levels showed carbamazepine of 5.9 mg/dL, valproate of 51.8 mg/dL, and phenobarbital of 42.0 mg/dL. Subsequent analysis revealed the presence of phenobarbital in Diankexing. No known anticonvulsants were detected in Diankening. Attempt to reduce the dose of Diankexing further resulted in increased frequency of seizures. She insisted in continue taking Diankexing and Diankening, although she was told that Diankexing contained phenobarbital.

## CASE REPORT 3

This 13 years old Chinese female was diagnosed to have Angelman's syndrome with moderate mental retardation, mutism and hyperactive behavior. She has seizures since infancy,

consisting of generalized convulsions. The seizures were catamenial, usually occurring in clusters about once a month. She attended special school. The main caregivers were her maternal grandparents, who were retired Chinese school teachers. Although she attended the hospital clinic regularly, and was prescribed sodium valproate, she did not take the medication. The main reasons given were the fear of side effects from sodium valproate, and the grandparents were also advised by the traditional Chinese physician not to mix the antiepileptic drug with traditional herbal medicine. The traditional herbal medicine prescribed were Diankexing and Diankening to be taken daily. Further analysis showed that both Diankexing and Diankening contained phenobarbital. After explaining to the grandparents the contents of the purported traditional medicine, the patient was treated with sodium valproate and lamotrigine, and Diankexing and Diankening were tailed off. In the subsequent months, the seizures became less frequent, and the hyperactive behavior also improved.

## DISCUSSION

This is a report of three patients purported to take traditional herbal medicine (Diankexing and Diankening) for treatment of epilepsy, which were adulterated with phenobarbital. Patient One developed phenobarbital toxicity. Patient Two had improved seizure control, but also showed mild ataxia probably contributed by phenobarbital. Patient Three had hyperactive behavior from phenobarbital.

Diankexing was said to composed of 20 medical herbs including *Arisaema consanguineum*, *Bambusa textilis*, *Saiga tatarica*, *Pteris martensii*, *Uncaria rhynchophylla*, *Bostaurus domesticus* (Gmelin), and others.<sup>4</sup> According to the labels in the packaging supplied to our patients, Diankexing contained Radix Salvia Miltiorrhiza, Arisaema Cum Bile, Margarita, Cornu Cervi Parvum, Fructus Pelargonium Graveolens, Succinum, and Calculus Bovis; and Diankening contained in addition, Radix Panacis Quinquefolii. None of the labels in the packaging mentioned that the purported traditional Chinese medicine contained phenobarbital.

There were previous reports of Diankexing being efficacious in treating epilepsy in both adults and children.<sup>3-5</sup> Although one of our patients (Case Two) showed improvement in seizure frequency with Diankexing, it was uncertain whether this was due to phenobarbital adulterated

in the preparation, or the traditional medicinal products. Adulteration of herbal products with prescription drugs and potentially dangerous substances has previously been reported in herbal products of Chinese and Indian origin.<sup>2,6-8</sup> Despite the potential benefit of traditional herbal medicine such as Diankexing and Diankening as effective anticonvulsants, the physicians should be aware of possible adulterations with conventional antiepileptic drugs, with potential adverse effects and drug interactions.

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