SHORT COMMUNICATION

Accelerated Elimination of Phenobarbital by Oral Activated Charcoal Suspensions with Alkaline Diuresis in an Overdose Patient

Nobuo INOTSUME*1 Akihiko KIMOTO*2 Hirotada KATSUYA*2 Masahiro NAKANO*1 and Akimasa HIGASHI*3

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*1 Department of Pharmaceutical Services, Kumamoto University Hospital, 1-1-1 Honjo, Kumamoto 860, Japan
*2 Intensive Care Unit, Kumamoto University Hospital
*3 Department of Pediatrics, Kumamoto University Medical School

A patient with phenobarbital overdose was treated with gastric administration of multiple doses of activated charcoal suspensions with alkaline diuresis. The decline of serum phenobarbital concentrations was sharper during the therapy than a control period. Elimination half-lives of phenobarbital of 15.5 and 39.1 h were obtained for the period of charcoal treatment with and without alkaline diuresis, respectively. As a normal elimination half-life of the patient was 82.2 h, combined use of oral activated charcoal with alkaline diuresis proved to be an effective, safe, and inexpensive therapeutic measure in a case of phenobarbital overdose.

Key words: phenobarbital, overdose, activated charcoal, alkaline diuresis, elimination half-life

Introduction

Multiple oral doses of activated charcoal have been shown to accelerate elimination of certain drugs and shorten duration of intoxication due to overdosed drugs. Neuvonen et al. reported that the elimination half-life of phenobarbital was decreased to 19.8 h from the control value of 110 h when administration of activated charcoal was started even after gastrointestinal absorption of phenobarbital was practically completed, i.e., in the elimination phase. We also demonstrated accelerated clearance of intravenously administered phenobarbital by oral doses of activated charcoal in rats. Oral administration of multiple doses of activated charcoal to volunteers substantially increased total body clearance of phenobarbital by a factor of 2.8 and decreased its elimination half-life by a factor of 0.4. In phenobarbital-overdosed patients treated in the same manner, the elimination half-lives of phenobarbital were less than 24 h which was approximately 25% of the average elimination half-life of the drug.

A patient who had taken a large amount of phenobarbital was treated with multiple doses of activated charcoal suspensions in a saline laxative solution via a gastric tube and with lactate diuresis in addition to intensive care including a respiratory support. This charcoal and alkaline diuresis therapy seemed to have shortened the elimination half-life of phenobarbital and duration of coma.
Case Report

A 23-year-old female in a comatose state was admitted to a medical intensive care unit after ingestion of an unknown amount of a drug powder. The patient had no history of renal, hepatic, or gastrointestinal disease and apparently took no medication other than the drug before her hospitalization. The patient was intubated and put on a mechanical ventilator. Infusion of lactate-Ringer's solution, in which lactate plays a role of a urinary alkalizer, was started (Fig. 1). Vital signs of the patient were kept within normal limits with these treatments. A nasogastric tube was inserted and vigorous gastric lavage was performed. Both white powder stuck on the clothes of the patient and an extract of the gastric contents were identified to be phenobarbital. Therefore serum levels of phenobarbital were determined by a fluorescence polarization immunoassay system (TDX). Since the concentration of the first serum sample was 107.7 μg/ml which was already in the toxic range, the following enteral charcoal therapy was started in order to reduce further absorption of the drug. The patient was given activated charcoal (35 g, Japanese Pharmacopeial grade) as a suspension in sodium sulfate (20 g) solution; subsequently, the patient was given activated charcoal (5 g each) suspended in magnesium citrate (13.6 g) solution at 6 and 7.5 h after, and additional activated charcoal (35 g each) suspended in magnesium citrate (27.2–34 g) solution at 14, 17, 20, 23, and 28 h after the first charcoal dose (Fig. 1). Serum levels of phenobarbital of the patient were still gradually increasing at the time when the charcoal therapy was initiated, but began to decrease at 10 h after the first charcoal dose. Clinical condition of the patient was rapidly improved with rapid decline in the serum levels of phenobarbital (Fig. 1), and the patient woke up at 29 h after the first charcoal dose. The pH values of urine samples of the patient were 7 to 8 during the charcoal therapy (Fig. 1). No side effect was observed in the patient.

Discussion

The rate of phenobarbital elimination from the serum was increased by giving multiple doses of activated charcoal suspended in saline laxatives with lactate diuresis. An increase in serum phenobarbital levels in the patient despite initiation of the therapy may be attributed to absorption of phenobarbital already in the intestine when activated charcoal was still in the stomach and to a relatively small amount of the charcoal in the second and third doses.

A recent case study demonstrated that the elimination half-lives of phenobarbital were reduced to one-fourth of those expected in the absence of an activated charcoal therapy.6) A first order decline of serum concentrations of phenobarbital was observed in the patient, indicating that the present charcoal therapy was clinically effective even in high serum concentrations of phenobarbital. Assuming that the effect of alkaline diuresis continued to the time of an intersection point between the rapid and slow decline phases shown in Fig. 1, the values of 15.5 and 39.1 h were obtained by linear regression analysis as elimination half-lives of phenobarbital during the charcoal treatment with and without lactate diuresis, respectively. A normal elimination half-life of phenobarbital of the patient was 82.2 h, which fell within the reported range of 48–114 h, and pharmacokinetic consideration indicated that the elimination half-lives of phenobarbital during the fast and slow decline phases were 19 and 48%, respectively, of the normal value of the patient. Although Alvin et al.7) reported on biphasic decline of phenobarbital, a distribution phase of phenobarbital...
bital must have been almost completed in this case because ingestion of phenobarbital of the patient was estimated to be about 5 h before admission and the fast decline phase in Fig. 1 continued for two days after admission.

In the present case, elimination of the drug seems to have been more accelerated by combination of alkalization of the urine and adsorption by accelerated charcoal, than by alkalization of the urine alone which may double the elimination rate of the drug. The present results confirmed that activated charcoal not only inhibits absorption of the drug still in the gastrointestinal tract but also extracts the drug already in the blood stream to the intestinal tract, this is called "intestinal dialysis." The effectiveness of other medications might be decreased when used concurrently with activated charcoal because of their adsorption by activated charcoal. This drawback, however, might not be medically threatening.

In this case report, it is demonstrated that the combination therapy of administration of multiple doses of activated charcoal and alkalization of urine shortened the elimination half-life of phenobarbital in serum. Since this therapy is effective, safe, and inexpensive, it would be valuable in the early management of a phenobarbital overdose.

References