Successful treatment of theophylline toxicity by upper gastrointestinal endoscopy

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INTRODUCTION
Theophylline is widely used for the treatment of asthma. Since its therapeutic range is narrow (5–20 μg/ml), substantial toxicity can occur when used at a dose slightly higher than the therapeutic range. Gastrointestinal symptoms, headache and tachycardia are experienced with serum theophylline concentrations (STC) > 20 μg/ml, but severe adverse effects (e.g., ventricular arrhythmias, seizure and shock) are reported in patients with STC > 40 μg/ml (1,2). Theophylline toxicity is classified into acute and chronic; the former represents ingestion of a single high dose of theophylline; while the latter results from ingestion of multiple doses of theophylline associated with impaired theophylline clearance, prescription of high doses by physicians and inadequate ingestion. In comparison with chronic toxicity, acute toxicity is associated with higher peak STC, younger age, and greater mortality (3). We describe here a case of acute theophylline toxicity following ingestion of a large amount of theophylline in a suicide attempt. The patients recovered after removal of the tablets from the stomach by endoscopy.

CASE REPORT
A 28-year-old Japanese man with atopic severe persistent asthma visited our hospital at 7:50 pm on April 17, 2001 complaining of abdominal pain. He had been treated with sustained-release tablets of theophylline 400 mg/day (Otsuka Pharmaceuticals, Tokyo, Japan), leukotriene receptor antagonist pranlukast 450 mg/day (Ono Pharmaceutical, Osaka, Japan) and methyl prednisolone 4 mg/day (Japan Upjohn, Tokyo). Physical examination revealed systemic hypotension (90/48 mmHg), tachycardia (160/min) and finger tremors. Consciousness was clear but he was very irritable. Respiratory sound was normal. We suspected acute theophylline toxicity based on clinical symptoms and physical examination but the patient denied taking excessive amount of medicines. Emergency abdominal CT scan and upper gastrointestinal endoscopy were performed to investigate the cause of abdominal pain. Abdominal CT scan showed many tablet-shaped shadows in the stomach and small intestine (Fig.1, left). Furthermore, using a gastrointestinal endoscope we found many tablets of sustained-release theophylline in the stomach (Fig.1, right), in addition to mucosal laceration, bleeding, congestion and swelling at the esophago-gastric junction. The final diagnosis was acute theophylline toxicity. Because of the large number of tablets in the stomach, gastric lavage using a stomach tube was ineffective, rather endoscopic removal of whole 31 tablets in the stomach was performed using three-legged forceps at 10:00 pm. Later, the patient admitted ingestion of about 50 tablets of sustained-release theophylline at 5:00 pm, 3 h before admission. Since STC 12 h after ingestion was very high (100 μg/ml), he was treated with both overhydration using large amount of intravenous fluid and activated charcoal (30 g 6 times at intervals of 6 h). STC decreased rapidly (STC 23 and 44 h after ingestion were 66.9 and 8.1 μg/ml, respectively) and symptoms improved. Arrhythmia, seizure and other severe complications did not occur throughout hospitalization.

DISCUSSION
We described a case of attempted suicide and acute theophylline toxicity. Parr et al. (4) reported 64 cases of acute theophylline toxicity, who were all but two...
attempted suicide cases. Other causes of acute theophylline toxicity include prescription of high doses by physicians and accidental ingestion. Thus, prescription of theophylline should be accompanied by education of patients and/or their families about the potential dangers.

In contrast to chronic toxicity, peak STC correlates with the severity of acute theophylline toxicity. In one report, three patients of 14 cases of acute theophylline toxicity who later died had a peak STC of >100 μg/ml (3). In contrast, Parr et al. (4) examined 64 cases of acute theophylline toxicity and found no fatal cases even though peak STCs in 9 was >100 μg/ml. The peak STCs in our case was also 100 μg/ml but the patient showed full recovery without any serious complications. Thus, patients with high STC levels can recover with proper treatment.

In the present case, all tablets of sustained-release theophylline found in the stomach were successfully removed by endoscopy. To our knowledge, this is the first case of successful treatment of acute theophylline toxicity by endoscopy. The reason that STCs can remain high is continued absorption of theophylline as it is released from the sustained-release tablet, throughout the digestive tract. Sustained-release theophylline could remain in the stomach for 8–12 h in acute overdose (4). For example, Macdonald et al reported a case whose STC was 138 μg/ml after 36 h later of 50'Phylocontin'tablets (aminophylline, 225 mg slow release) ingestion (5). In the present case, all tablets found in the stomach could be removed soon after admission, which effectively prevented further rises in STC and also probably allowed the subsequent rapid fall in STC and saved the patients from potentially serious complications.

REFERENCES