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Ubretid (distigmine bromide) taken to treat urinary retention prolongs the effect of suxamethonium

Shiroh Isono[1], Kei Iizuka*, Goro Fukami[2], Norihiro Shinozuka[1], Masaomi Iyo[2], and Takashi Nishino[1]
[1]Department of Anesthesiology (B1), Graduate School of Medicine, Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba 260-8670, Japan
[2]Department of Psychiatry, Graduate School of Medicine, Chiba University, Chiba, Japan

To the editor: We recently experienced prolongation of the effect of suxamethonium in a patient with depression who was taking distigmine bromide (Ubretid; Torii Pharmaceutical, Tokyo, Japan), an anticholinesterase drug, for the treatment of urinary retention caused by a tricyclic antidepressant.

A 42-year-old man was scheduled for electroconvulsive therapy (ECT) for depression. Responses to propofol ($1.5\ mg \cdot kg^{-1}$) and suxamethonium ($1\ mg \cdot kg^{-1}$) were normal and ECT was performed successfully. The anesthetist, however, encountered difficulty in the restoration of spontaneous breathing despite an end-tidal carbon dioxide increase of up to 70 mmHg. Hiccup-like diaphragm contractions emerged 15 min after suxamethonium administration, with no adequate ventilation established. The potential development of a phase II block was confirmed by the absence of response to train-of-four electrical stimulations at the ulnar nerve. Full recovery of ulnar nerve electrical stimulation and adequate spontaneous breathing was obtained approximately 30 min after suxamethonium administration. A thorough investigation performed after this ECT revealed regular oral administration of Ubretid ($15\ mg \cdot day^{-1}$ for approximately 8 months) as the potential cause of the prolongation of the effect of suxamethonium. The patient had taken 5 mg Ubretid 4 h before the induction of anesthesia. Although blood sample testing was not performed at the time of the complication, a relatively low plasma cholinesterase level was revealed the following day ($137\ U \cdot l^{-1}$), and the level was normalized a week after the cessation of Ubretid ($293\ U \cdot l^{-1}$) (normal range at our institute, 180 to $430\ U \cdot l^{-1}$). We did not consider the involvement of atypical pseudocholinesterase, and no genotypes were identified. A second ECT was uneventfully performed after the cessation of Ubretid.

Ubretid is commonly prescribed for the treatment of myasthenia gravis and for difficulty in emptying the bladder. Because of its anticholinesterase effect, Ubretid inhibits plasma cholinesterase activity; it therefore delays the hydrolysis of suxamethonium and prolongs its action, similar to the effects shown by other anticholinesterase drugs, such as pyridostigmine (used for the treatment of myasthenia gravis) and donepezil (used for the treatment of Alzheimer's disease) [1,2]. Of note, serum concentrations of acetylcholinesterase and pseudocholinesterase were reported to be decreased in patients, with adverse cholinergic effects, caused by treatment with Ubretid [3]. Accordingly, a decrease in plasma cholinesterase levels caused by regular medication with these agents may also contribute to the delayed metabolism of suxamethonium by plasma cholinesterase. Because of the apparent pharmacological interaction between Ubretid and suxamethonium, pharmaceutical company alerts not to administer suxamethonium to patients treated with Ubretid. We advise anesthesiology colleagues not to overlook a medication history of Ubretid, particularly upon suxamethonium administration.

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Address correspondence to: S. Isono
*K. Iizuka is a student at the School of Medicine, Chiba University, Chiba, Japan.
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