Metoprolol for Intermittent Explosive Disorder

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Metoprolol, a selective β_1-adrenoreceptor blocker, was administered to two patients with intermittent explosive disorder who had not done well with previous medications, including propranolol and carbamazepine. Both patients improved dramatically, suggesting clinical and theoretical relevance.
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Metoprolol, a selective β_1-adrenoreceptor blocker, has not, to my knowledge, been previously reported to be useful for intermittent explosive disorder. In the course of a study evaluating propranolol and carbamazepine for temper outbursts, I encountered two patients who were not sufficiently helped by either medication; metoprolol produced gratifying results. Metoprolol was chosen because it is one of the few β blockers on the market that crosses the blood-brain barrier.

The efficacy of another β blocker, propranolol, for temper outbursts was initially reported by Elliott (1), who studied seven adults with temper outbursts that began after acute brain damage. Yudofsky et al. (2) then reported improvement in four patients with more chronic brain dysfunction and episodic belligerence, and Williams et al. (3) reported 75% improvement among 30 children and adolescents with uncontrolled rage outbursts and concomitant brain dysfunction who received up to 1600 mg/day of propranolol. A Massachusetts General Hospital newsletter (4) summarized six studies and concluded that propranolol in doses up to 320 mg/day reduces violent behavior in elderly patients with known brain damage.

CASE REPORTS

Case 1. Mr. A, a 30-year-old divorced white postal worker, had a 10-year history of temper outbursts, episodic alcohol abuse, and tremor; he had had meningitis at age 2. Extensive previous neurological evaluation, including two CAT scans, several EEGs, two lumbar punctures, and measurement of plasma ceruloplasmin, had produced negative results; a more recent CAT scan indicated mild atrophy, which was attributed to his alcoholism. During his temper outbursts Mr. A would "rant and rave like a madman," threatening others to the extent that his supervisor at work locked himself in a room to avoid harm; the outbursts occurred about every other day. There was always a precipitant, although it could be a minor stress; there was no amnesia, and Mr. A felt guilty afterward. Alcohol at times worsened his temper, but at other times he drank to reduce anxiety, which might lead to an outburst; most outbursts occurred when he was sober. Aside from his outbursts, he was pleasant and likable; however, his outbursts were a major reason for his divorce and were jeopardizing his job.

A year before admission Mr. A had taken propranolol (100 mg q.i.d.) for several months with significant benefit, but he became depressed while taking propranolol, so it was discontinued. He had also received two trials of carbamazepine (200 mg t.i.d.) for his temper with evidence of benefit, but both times he developed a severe rash, requiring discontinuation, within 2 weeks. After the second trial of carbamazepine he was given metoprolol, 50 mg b.i.d.; the dose was gradually increased to 100 mg in the morning and 200 mg h.s. There was a marked response; his outbursts became less frequent and less severe. Psychiatrist, patient, and girlfriend agreed that Mr. A was very much improved. Follow-up 7 months after discharge showed continued benefit from the same dose, with relative sobriety and a reduction in his tremor. A 2-week trial without metoprolol resulted in increased irritability, temper, and tremor.

Case 2. Mr. B, a 35-year-old married unemployed white man, had always been hot-tempered but developed discrete rage outbursts after a shotgun accident 6 years before admission. During his temper outbursts, for which he was totally amnestic, he attempted to beat, rape, and/or sodomize his wife and children. Despite his size (295 lb.) and his green belt in karate, he had never hurt anyone because he "lost his strength" during these outbursts and his wife could fend him off. His wife indicated that he was irritable for 1–2 days before an outburst; during an episode his eyes were "milky" and he did not respond to orders or questions.

During Mr. B's accident one shotgun pellet penetrated the left frontal region of his brain, traversed the thalamus and the third ventricle, and lodged in the right posterior temporal region. Neurological sequelae included a left hemiparesis with increased left-sided reflexes; he also developed diabetes insipidus and low testosterone levels. CAT scan showed scar formation in the right temporal and left frontal regions, with some evidence of hydrocephalus, but the CAT results had been stable for the past 5 years. An EEG with nasopharyngeal leads was normal.

The temper outbursts, occurring about once every 2 weeks, were diagnosed originally as temporal lobe epilepsy and treated with carbamazepine, 800 mg/day (with a blood level of 9 μg/ml), and valproic acid (to a blood level of 49 μg/ml). About 2 years before admission propranolol, 40 mg q.i.d., was added to the carbamazepine for 2 months, but the

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dose was limited by sedation. None of these medicines had clearly helped, but Mr. B was still taking carbamazepine, 800 mg/day, at admission. Metoprolol, up to 100 mg b.i.d., was then added to the carbamazepine, and he improved. Follow-up 11 months later, with no change in medication, showed him to be doing well according to himself, his wife, his parents, and his psychiatrist. He had had only one outburst, with amnesia, over the 11 months.

DISCUSSION

Both patients met the *DSM-III* criteria for intermittent explosive disorder, but in both cases the etiology was unclear. Mr. A had a history of meningitis and tremor and had a CAT scan that showed mild atrophy, while Mr. B had evidence of temporal lobe epilepsy. The generalizability of these results, therefore, is uncertain.

These vignettes, however, suggest that metoprolol may be helpful for patients with intermittent explosive disorder. Since metoprolol blocks β_1, but not β_2, receptors and does not have propranolol's membrane-stabilizing effect, these results, if confirmed, may have implications regarding the mechanism of action of β blockers on rage outbursts. From a clinical perspective, reduced side effects, e.g., less blockade of the β_2 receptors needed for treating bronchospastic disease, might be the main advantage of metoprolol over propranolol. Controlled studies to evaluate the efficacy of metoprolol for patients with rage outbursts are needed.

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