Baclofen in the Treatment of Stiff-Man Syndrome

Frank Miller, MD, and Holly Korsvik, MS

Baclofen, 90 mg daily, was given to a patient with stiff-man syndrome diagnosed by electromyography and clinical criteria. The patient, bedridden for three years, experienced a decrease in rigidity, cramping, stiffness, and spasm and was able to walk on the thirtieth day of treatment.

Miller F, Korsvik H: Baclofen in the treatment of stiff-man syndrome. Ann Neurol 9:511–512, 1981

Stiff-man syndrome is characterized by episodic aching and tightening of the axial musculature. Over time the tightness becomes constant, spreads to the limb girdles, and renders volitional movement virtually impossible since simultaneous involvement of antagonistic muscle groups makes motion at joints extremely difficult. Associated with the persistent rigidity of muscles are paroxysms of muscle spasms of such intensity that the patient appears to be in a shocklike state of diaphoresis, tachycardia, and restlessness with elevated blood pressure. Spasms last several minutes and are followed by periods of disorientation, discomfort, and fear. Rigidity is abolished during sleep, but sensory stimuli great enough to disturb sleep precipitate spasms and generalized autonomic discharge. Intellect is generally preserved, although one investigator found deterioration [1]. Except for difficulty in active movement and the rigid musculature, normal reflex and sensory examinations are the rule. The diagnosis of stiff-man syndrome is established by the presence of the characteristic clinical signs and an electromyographic (EMG) pattern of persistent tonic contractions reflected in constant firing even when the patient is attempting to relax [5]. The action potentials themselves are unremarkable. However, no amount of relaxation is capable of completely silencing the resting EMG.

Howard [4] introduced the use of diazepam in the management of stiff-man syndrome. He achieved functional improvement in the status of three patients. Furthermore, with diazepam therapy, EMG revealed electrical silence at rest. Unfortunately, the amount of diazepam needed to produce functional improvement often is associated with profound sedation.

Gordon et al [3] hypothesized that persistent extrafusal muscle contractility was maintained by abnormal activity of the gamma motor neuron system. γ-Aminobutyric acid (GABA) is the putative inhibitory transmitter in this system [2]. As such, its relative absence or unavailability may account for the rigidity and spasm encountered in stiff-man syndrome. With this in mind, we used Baclofen (4-amino-3-[*p*-chlorophenyl] butyric acid), an analog of GABA, in the management of a case of stiff-man syndrome treated symptomatically with diazepam in the past but complicated by excessive sedation.

A 68-year-old black woman was admitted to Cleveland Metropolitan General Hospital in May, 1980, at the request of her family, who stated that she was febrile, disoriented, and bedridden. She had been in good health until 1972, when she noticed episodes of stiffness and tightening in her legs. The episodes occurred infrequently at first, but by 1976 were occurring daily and necessitated the use of a cane. In 1977 she stopped working and retreated to bed. Diazepam, 40 to 60 mg per day in divided doses, was prescribed. During this period the stiffness and rigidity were complicated by painful spasms of the lower back and legs. Intense spasms triggered by noise, jarring, attempts at voluntary novement, or emotional stress would last from 10 to 30 minutes and were associated with diaphoresis. Over the preceding year the spasms had been of such intensity that the patient became disoriented during the episodes. In early 1980 the patient stopped taking diazepam, fearing addiction.

Physical examination revealed a well-developed black woman lying rigidly in bed. Vital signs were normal. She weighed 55 kg. There were no distortions of her hands or feet, though her feet were dorsiflexed. Muscles were stony hard, with rigidity of the thighs, calves, and lower back. No muscle tenderness or fasciculations were present. The patient could move her arms, but her legs and back were rigidly immobile. Attempts to raise her to a sitting position in bed produced boardlike stiffness, spasm, pain, disorientation, and emotional incontinence.

On neurological examination the patient was alert and oriented to time and person, though not to place. Cranial nerves were intact. There was no sensory deficit. The deep tendon reflexes were normal and there was no Babinski sign. Routine chemistry determinations including muscle enzymes, transaminases, electrolytes, calcium, and phosphorus were normal. The complete blood count was remarkable for anemia of the chronic disease type; sickle cell preparation was positive (showing hemoglobin AS).

During the first two weeks of her hospital stay the patient experienced intense muscle spasms when frightened or stimulated by noise, jarring, eating, or passive movement. An EMG demonstrated tonic motor unit activity at rest. The electrical activity was augmented by passive stretch and motion. Her symptoms were not completely relieved by 40 to 60 mg of diazepam per day. For this rea-

From the Department of Psychiatry, Cleveland Metropolitan General Hospital, 3395 Scranton Rd, Cleveland, OH 44109.

Received Oct 22, 1980, and in revised form Nov 7. Accepted for publication Nov 11, 1980.

Address reprint requests to Dr Miller.

son, the patient was started on baclofen at increasing daily dosages of 15, 30, 45, and 60 mg for three days at each increment, and then 90 mg per day in divided doses. She suffered no side effects and by the fourteenth day of treatment was no longer experiencing cramps or spasms. The associated shocklike syndrome disappeared, as did much of her disorientation. On the eighteenth day of treatment the rigidity disappeared. The patient was so fearful voluntary movement would precipitate a crisis, however, that she was unwilling to sit up in bed until the twenty-eighth day of treatment. After that she rapidly progressed to sitting and then walking with assistance.

The hospital course was complicated by intercurrent urinary tract infections, which did not produce relapses.

Discussion

Gordon et al [3] developed the hypothesis that the continuous alpha motor neuron activity encountered in stiff-man syndrome is maintained by abnormal activity of the gamma motor neuron system caused by a persistent suprasegmental drive. Increased afferent discharge from stretch receptors in the muscle spindles reflexly produces constant firing of the alpha motor neurons, and thus tonic rigidity of voluntary muscles. Howard [4] speculated that continuous motor unit activity arises from loss of inhibitory action of interneurons. Since GABA is regarded as an inhibitory neurotransmitter, it is noteworthy that baclofen, an analog of GABA, modified our patient's symptoms. Thus, we speculate that relative absence or unavailability of GABA may account for the symptoms encountered in stiff-man syndrome. Whether the persistent discharge of the anterior horn cells is due to dysfunction of the inhibitory interneurons or to a persistent and abnormal drive delivered to the gamma motor neurons from suprasegmental sites (e.g., cerebellum or reticular activating system) remains to be determined.

References

1. Asher R: A woman with stiff-man syndrome. Br Med J 1:265–266, 1958
2. Goodman LS, Gilman A: The Pharmacological Basis of Therapeutics. Fifth edition. New York, Macmillan, 1975, pp 431–432
3. Gordon EE, Janusko DM, Kaufman L: A critical survey of stiff-man syndrome. Am J Med 42:582–599, 1967
4. Howard FM: A new and effective drug in the treatment of stiff-man syndrome. Proc Staff Meet Mayo Clin 38:203–212, 1963
5. Moersch FP, Woltman HW: Progressive fluctuating muscular rigidity and spasm (stiff-man syndrome). Proc Staff Meet Mayo Clin 31:421–427, 1956