The Value of Mephenesin Carbamate in the Control of Pain in Patients with Tic Douloureux*

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leviation of the pain of tic douloureux has been attempted with many non-narcotic pharmacologic agents. Few have remained in common use for long. Vitamin B12, 6, 13, 25 hydantoin derivatives, 4, 7, 8, 12, 19, 22, 24 G 32883, 3, 8 and mephenesin carbamate suspension 9 have been used in recent years.

The rationale for the selection of mephenesin for this purpose was speculative. It had been noted in cats that small intravenous doses of mephenesin reduced the amplitude of the trigeminal dorsal root reflex and the overreaction to tactile facial stimulation, incident to the application of strychnine to the surface of the medulla overlying trigeminal nucleus caudalis. 10 Without great expectations, intravenous mephenesin was administered to 2 patients with severe tic douloureux. Their facial pain stopped for 1/2 to 1 1/2 hours after each injection. Because of its low toxicity and the infrequency of serious side effects associated with the use of mephenesin, 1, 2, 17, 18, 21 further efforts to control the pain of tic douloureux with this drug seemed warranted.

In 1959, we made a preliminary report describing the use of mephenesin in the management of 29 patients with tic douloureux. 9 At the end of a one-year trial period, 10 patients reported no pain, 12 had mild pain, and 4 had moderate pain despite continuing medication. One reported no improvement. Two had been operated upon.

The present report describes the results of a 7-year study of 52 consecutive patients treated for tic douloureux with mephenesin carbamate suspension.

Clinical Material

Each of the 52 patients in this study had paroxysmal pain in the distribution of the trigeminal nerve without evidence of trigeminal deficit except for that which might be related to previous operative procedures on the trigeminal system. Trigger points were noted in all but two.

The distribution of patients by sex and age was comparable to the characteristics of the disease. Pain occurred on the left side in 17, on the right in 27 and bilaterally in 8 patients.

The duration of symptoms prior to this form of management extended for less than 1 year in 13 patients, 1–5 years in 20 patients, 5–10 years in 7 patients and for more than 10 years in 12 patients.

Twenty-three patients had had previous operative procedures in attempts to control their pain. As a result of these procedures, 8 had a mild sensory deficit, 3 had extensive sensory deficit and 1 had total anesthesia in the 2nd and 3rd divisions of the trigeminal.

Each patient was examined for lesions in the head or neck which might contribute to the production of face pain. Three patients underwent correction of dental malocclusion and others required treatment for malfitting plates or dental caries. Several patients had chronic recurrent sinusitis and 3 others had respiratory infections. X-rays of the skull were normal in each instance.

Two patients died in the course of this study, 1 after a cerebrovascular accident at the age of 74 and one at age 73 following a “heart attack.” These 2 patients had been maintained without an operative procedure for 4 and 5 years and are included as 4 and 5 year follow-ups, respectively.

Method of Management

The method of management evolved as a relatively standard pattern. Each patient was initially given 1 gm. (1 teaspoon) of mephenesin carbamate suspension every 3 hours to determine the extent of any side effects at a low dose during the next 24 hours. On the 3rd day each received 3 gm. every 3 hours. They were maintained on this dose as pain gradually subsided over a period of from 3 days to 2 weeks. On rare occasions, for periods of several days, patients received as much as 5–9 gm. every hour. Two patients received as much as 8 gms. of mephenesin carbamate every 3 hours for many months.

Twenty patients who experienced severe exacerbations and were unable to take oral medication were admitted to the hospital for

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intravenous medication with mephenesin. One patient was hospitalized for this reason on 3 occasions. Four grams of mephenesin were added to 5% glucose in distilled water to a total volume of 500 cc, and this was administered by slow intravenous drip over a period of 12 hours. In several instances, 6 gm., and in one instance, 8 gm. I.V. in 12 hours, were required to control pain. The intravenous drip was maintained with a catheter for 48-72 hours. Oral medication was continued. At the termination of the intravenous medication, the patients were discharged on oral medication.

Twenty patients who experienced an exacerbation after a remission were placed also on diphenylhydantoin sodium, 100 mg., t.i.d. for brief periods. Eight have remained on both drugs for longer intervals.

When a patient no longer experienced satisfactory control of pain and was inordinately disturbed by the side effects, an operative procedure was performed.

**Effect of Drug Therapy Only**

For purposes of this report the success or failure of the medical management of these patients has been judged in terms of the need to resort to an operative procedure for pain control.

*Oral Mephenesin Carbamate Suspension.* Those who remained under satisfactory control without further surgery took medication for varying periods of time. One was under observation for less than 6 months, 3 were under observation for from 6 to 12 months, 6 were treated for from 1 to 2 years, 9 were under observation for from 2 to 4 years, and 12 were followed for from 4 to 7 years.

The duration of symptoms prior to the initiation of medication may have had some bearing on the success or failure of this form of management. Ten of the 13 (77%) who had had symptoms for less than one year were controlled on medication only, 14 of the 20 (70%) with symptoms from 2 to 5 years were controlled without surgery, 2 of the 7 (29%) with symptoms from 5 to 10 years were controlled with drugs alone and 6 of the 12 (50%) with symptoms for more than 10 years required further operative procedures for pain control.

The incidence of failure to control pain with drugs alone was not affected by age, previous surgical treatment or the presence of postoperative sensory deficit.

Many patients with pain control on medication reported painless paroxysmal paresthesiae similar to “Gasserian ghosts” described by Pennan. They described these with some difficulty using one or more of the following terms: prickle, tingle, prick, throb, knock, quiver, jab, sparkle, touch, snap, twitch, flicker or bump. As their pain subsided during the first 2 weeks of treatment it was frequently replaced by these painless feelings, which occurred in the same distribution and had the same duration characteristic of their pain. They could, on occasion, be evoked from trigger points. Several patients came to consider recurrence of painless paroxysmal paresthesiae as a warning of an impending exacerbation of pain. Their medication was increased until the paresthesiae subsided.

Non-paroxysmal persistent paresthesiae were reported by 28 patients who described them as: sore gums or lips, crawling, burning, aching, stinging, pressure, gnawing, pinching, swollen cheek or lip, stiff lip or tongue, tingling and prickling or creeping. Seventeen had had previous operative procedures and 14 ultimately required another operative procedure for pain alleviation. The paresthesiae have persisted in each instance. Among the 11 who had not previously been operated upon, the paresthesiae were mild and intermittent. In no instance did they become a major problem in the patient’s management.

*Mephenesin Carbamate Suspension plus Diphenylhydantoin Sodium.* During acute exacerbations of pain, 20 patients were placed on supplemental diphenylhydantoin sodium, 100 mg., t.i.d. Twelve reported less pain after several days but were also taking larger doses of mephenesin at these times. Eight remained on continuing medication with both drugs for extended periods of time and felt more confident of having less pain in this circumstance. This group, however, is too small to compare the numbers requiring surgical intervention as compared to the whole group under observation.

*Intravenous Mephenesin.* An acute exacerbation of pain could be brought rapidly under full control by an adequately titrated dose of intravenous mephenesin. In the group of 20 patients thus treated, only 1 patient failed to report total alleviation of pain soon after the initiation of an adequate drip. This patient was an elderly amputee with severe emotional disturbance. He received a maximum intravenous dose of 4 gm. in 12 hours.