

The treatment of 'shooting' pain

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Summary

Anticonvulsant drugs were given to 70 patients suffering from lancinating pains of various clinical aetiologies. Serum drug estimations were used to ensure that an effective dose level was achieved. In about 66% of the cases, treatment produced some diminution in the intensity and/or frequency of the 'flashes' of pain. The neurophysiological and pharmacological rationales are briefly explained. It is concluded that this use of anticonvulsant agents merits further study.

Introduction

The discovery that diphenylhydantoin (Braham and Saia, 1960) and carbamazepine (Blon, 1962) would effectively relieve the pain of trigeminal neuralgia and glossopharyngeal neuralgia (Bonduelle, *et al.*, 1964) opened a new dimension in the treatment of pain. More recently a number of isolated reports have appeared which suggest that these and other anticonvulsant drugs may perhaps be effective in a much wider range of painful conditions which involve pains of a shock-like, 'shooting' or 'flashing' nature. These may be associated with a 'trigger' area (such as a neuroma) light stimulation of which can set off an attack, but they often occur apparently completely spontaneously. The pains usually start suddenly and finish suddenly and are often brief in duration; they may occur as single 'flashes' or as machine-gun bursts. They usually occur in the same place every time and they may be accompanied by muscular contractions. Such pains are features of what Loeser (1975) called 'episodic central pains', tabetic lightning pain (Alajouanine, Thurel and Brunelli, 1936), and denervation hyperpathia (Gibson and White, 1971), diabetic neuropathy and neuropathies associated with neoplasms (Cambier and Dehen, 1971). A type of paroxysmal abdominal pain has been reported which was said to be a result of focal epilepsy and was found to respond to treatment with anticonvulsants (Peppercorn *et al.*, 1978).

Material and methods

For some time the author has been assessing the value of diphenylhydantoin (phenytoin-epanutin) and sodium valproate in a wide range of painful conditions all of which had in common the presence of pain of a spasmodic, 'shooting' nature. In addition to the 'shooting' pains there was frequently also a constant aching, burning or background discomfort. In many of the patients acute pain could be produced by pressure or tapping over a scar or the involved nerve.

Patients referred to the North West Regional Pain Relief Centre who on initial consultation were found to have such lancinating pains were started on diphenylhydantoin 50 mg thrice daily or sodium valproate 200 mg thrice daily. The patient was seen at intervals of 2 or 3 weeks thereafter and on each occasion response to treatment and occurrence of side effects were elicited. At each visit a blood sample was taken for serum drug estimation. In the absence of adequate suppression of the 'shooting' pains, the daily dose of phenytoin or valproate was increased (by 50 mg or 200 mg respectively) until effective relief was achieved or until an adequate blood level of the drug was attained. If little or no pain relief was obtained in the presence of an adequate blood level of one of these drugs or if intolerable side effects occurred and persisted, the patient was transferred to the other anticonvulsant drug.

Many of the patients with long-standing pain were suffering from depression as is commonly the case. These patients were given a combination of a tricyclic antidepressant with a phenothiazine agent (usually clomipramine + pericyazine or amitriptyline + perphenazine) in addition to the anticonvulsant agent.

Results

The results from 70 patients form the basis of the present interim report; 38 were female and 32 male. Table 1 shows the age range; Table 2 analyses the

TABLE 1. Age of patients

Age (in years)	11-20	21-30	31-40	41-50	51-60	61-70	71-80
No. of patients (/70)	2	2	15	15	15	15	6

cause of the pain. At the time of the first consultation, the pain had been present for a mean of 5 years ranging from 4 months to 33 years. In 16 patients the lancinating flashes of pain were accompanied by muscular twitches, spasms or jerks in the affected region.

Anticonvulsant therapy produced a distinct improvement in 67% of the patients. It must be understood that this implies a reduction in the frequency and/or intensity of the painful shoots only; the background continuous ache or pain was usually unaffected and the benefit appreciated by the patient depended on what proportion of his total pain was 'shooting' in nature. In all 16 patients with muscular contractions, anticonvulsant medication resulted in a reduction in the frequency and/or violence of the contractions. In some patients the tenderness over the affected nerve lessened.

The blood level of epanutin achieving good suppression of lancinating pain ranged from 11 to 44 $\mu\text{mol/l}$ with a mean of 24.4 $\mu\text{mol/l}$. The mean effective blood level of sodium valproate was 385.6 $\mu\text{mol/l}$ (range 190 to 550 $\mu\text{mol/l}$).

Thirty-four of the patients are now settled on valproate and 33 on epanutin. In 3 patients, neither drug was effective and carbamazepine is being employed. In 24 patients a change of drugs had to be effected either because of intolerable side effects or of inefficacy of the initial agent.

The complications encountered in this series were one or more of the following:

Depression	(1 valproate)
Nausea and gastric irritation	(7 valproate, 2 epanutin)
Drowsiness	(4 valproate, 3 epanutin)
Dizziness	(4 valproate, 3 epanutin)
Headache	(1 valproate)
Stomatitis	(1 valproate).

The side effects usually diminished with continued medication. Nausea and gastric irritation were often relieved by giving an anti-emetic or magnesium trisilicate; in the case of sodium valproate, relief could usually be achieved by changing to enteric-coated capsules.

Discussion

The present study shows that effective medication with some anticonvulsant drugs can markedly reduce the episodic pain which occurs in a number of different clinical conditions.

The neurophysiological basis for this type of pain has recently been studied by a number of workers. Shoots of pain not infrequently follow intraspinal injury to the spinal cord or nerve roots; in fact the incidence has been reported to be as high as 10% (Gibson and White, 1971). Cambier and Dehen (1976) showed that 'lightning' pains developed a few weeks or months after rhizotomy or destruction of one or 2 neighbouring nerve roots and suggested that the pains are due to suppression of the inhibitory action of myelinated fibres. Wall (1979) reports that disorders which primarily affect the dorsal root ganglion cells may involve peripheral axons extending centrally into the CNS as well as peripheral ones.

TABLE 2. Cause of pain

Cause of pain	No. of cases
Post-laminectomy	13
Post-operation neuralgia (nerve entrapment, neuroma, painful scar)	11
Post-amputation neuralgia	10
Post-herpetic neuralgia	9
Nerve/plexus injury or operation	7
Post-traumatic neuralgia	7
Central pain	5
Trigeminal neuralgia	3
Neoplastic neuropathy	2
Atypical facial pain	2
Scleroderma	1
Total	70

Loeser and his colleagues (Loeser, Ward and White, 1968) found cells in the cortex with periodic abnormal bursts of firing following afferent denervation of the grey matter of the dorsal horn of the spinal cord. Loeser (1975) postulates that episodic central pains are the equivalent of focal cortical epilepsy occurring in a cutaneous sensory system. It is interesting to note that, as long ago as 1959, trigeminal neuralgia was called 'epileptiform neuralgia' by Kugelberg and Lindblom (1959).

From a pharmacological viewpoint, diphenylhydantoin (DPH) seems to exert a stabilizing effect on many excitable membranes. It has been shown to reduce post-tetanic potentiation at synapses within the spinal cord (Esplin, 1957). DPH can block increased excitability to supramaximal rapid stimuli or repetitive firing following a single shock in experimental nerve preparations. It also stabilizes against hyperexcitability caused by a low calcium level or various drugs. This stabilizing effect is shared by other anticonvulsants with a phenyl or

equivalent aromatic ring (Toman, 1970). Morrell, Bradley and Petashne (1958) studied rabbit posterior tibial nerve and found that i.v. DPH increased its threshold to stimulation and synaptic delay and/or conduction time. This led to the use of DPH in trigeminal neuralgia and glossopharyngeal neuralgia.

DPH does not elevate the threshold for minimal electroshock seizures produced by convulsants; it strikingly limits the development of maximal seizure activity from a discharging focus without necessarily influencing the focus itself (Toman, 1970).

A good correlation has been found between serum and brain level of DPH (Sherwin, Wisen and Sokolowski, 1973). Unreliable intake and drug interaction are important factors affecting the serum level of anticonvulsants. Monitoring of the blood level during treatment is important because serum estimations enable one to identify pharmacologically adequate dosage as well as to identify patients who are not taking their medication.

Dunsker and Mayfield (1976) report 5 cases of 'shooting' pain which were treated with carbamazepine; in 3 'acute' cases (all immediate post-laminectomy) it was possible to discontinue the medication after only a few days without recurrence of pain. In the present series all the patients had chronic pain and discontinuation of therapy has been found possible in only one patient; in a second patient a maintenance dose of 200 mg valproate has been satisfactory over a follow-up of 10 months. In all other cases a 'full' dose has had to be continued to avoid recurrence of pain. On a blood level of drug which is subtherapeutic for control of epilepsy this would appear to be a safe procedure. The unpredictable and severe metabolic injury to liver function in relation to sodium valproate (Suchy *et al.*, 1979) suggests that diphenylhydantoin is preferable from the side effects standpoint.

Failure to respond was observed in 33% of the present patients, reflecting probably multiple factors not wholly clear at this stage of this continuing investigation. Further work needs to be done to clarify these points and this would obviously include EEG studies. The relative value of carbamazepine and clonazepam in these types of cases is now being studied. Finally, anticonvulsants have been claimed to provide pain relief in conditions where there is no element of 'shooting' pains (Raskin *et al.*, 1974; Freidman, 1968; Mladinich, 1974). This obviously deserves closer investigation.

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