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Intravenous Diazepam in Drug-Induced Dystonic Reactions

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Acute dystonic reactions, including oculogyric crises, were once thought to be pathognomonic of encephalitis lethargica, but the clinical use of the phenothiazines has led to the recognition that similar symptoms can be produced by these drugs. Some phenothiazines, such as trifluoperazine, fluphenazine, prochlorperazine and perphenazine (Ayd, 1960; Christian and Paulson, 1958; Hollister, 1957; Waugh and Metts, 1960), are thought to cause these effects more frequently, especially when given parenterally. Other non-phenothiazine tranquillizers, for example haloperidol, also produce these reactions. not un-commonly. Certain patients, particularly the young and perhaps the genetically predisposed, are more likely to be affected.

The dystonic postures may present in different ways, among which the most common is spasm of muscles of the neck. Oculogyric crises occur either in isolation or in combination with other forms of dystonia. In severe reactions most voluntary muscles of the body are involved, and if laryngospasm occurs alarming dyspnoea endangering life may result (Waugh and Metts, 1960; Smith and Miller, 1961). These reactions, although not uncommon, may suggest false diagnoses, ranging from meningoencephalitis (e.g. in a child suffering from fever and vomiting treated with perphenazine) to conversion hysteria and tetanus (Gleckman *et al.*, 1969).

A quick, safe and effective method of treatment of such disorders is highly desirable, and such a method would also provide a useful diagnostic tool.

Many different drugs have been used to relieve these symptoms, including oral acetylsalicylic acid and amphetamine, and intravenous calcium gluconate, diphenylhydantoin, caffeine and narcotics (Herz and Meyers, 1955; Freyhan 1958; Goldman, 1958; Montgomery and Sutherland, 1959; Smith and Miller, 1961). All these have been discarded as unreliable or too slow-acting. Anti-parkinsonian anticholinergic drugs (Freyhan, 1958; Goldman, 1958; Ayd, 1960; Smith and Miller, 1961), and antihistamines (Smith and Miller, 1961; Gleckman *et al.*, 1969) are usually effective, but may themselves produce misleading mental and other unpleasant side effects (Stephens, 1967). However, the response—even to such drugs as procyclidine and biperiden—is by no means constant and may only be temporary (Christian and Paulson, 1958; Paulson, 1960; Waugh and Metts, 1960; Smith and Miller, 1961). Barbiturates are helpful if given intravenously, but intramuscular use is unreliable, and as these patients are already predisposed to laryngeal spasm these drugs may be hazardous. Moreover, the beneficial effects of the barbiturates are often accompanied by marked sedation. In fact, induction of sleep is held by some to be therapeutically important (Chamberlin and Trembly, 1965). The sedation may blur the clinical picture, for example if encephalitis is being considered in the differential diagnosis.

We wish to report the use of intravenous diazepam in drug-induced dystonias, with favourable results. The drug has been used by us in several cases, without any complications, and three examples are given. As far as we know, a similar use of diazepam has been recorded previously only in a single case of bucco-oro-lingual dystonia (Davies, 1970) and never in other types of drug-induced dystonias.

Case Reports

Case 1. A.F. was a 23-year-old single man suffering from schizophrenia with well marked thought disorder, passivity feelings and persecutory delusions. He had been ill for six years and had been treated with phenothiazines of different kinds both as in-patient and as out-patient. When first treated with chlorpromazine he developed agranulocytosis, but recovered when the drug was withdrawn. He then received trifluoperazine, but this was replaced by

fluphenazine enanthate 25 mg. intramuscularly every three weeks, as he did not take oral medication regularly. While on fluphenazine, and although also receiving orphenadrine 50 mg. t.i.d., he twice developed oculogyric crises on the second day after injection of fluphenazine. His eyes deviated to the right and upwards, and this was accompanied by rotation of his head to the right. The attacks responded within minutes to 10 mg. of diazepam intravenously.

Case 2. N.H. was a 45-year-old married woman suffering from a long standing obsessional ruminative state, at times accompanied by moderately severe depressive symptoms. She was treated with monoamine oxidase inhibitors and tricyclic antidepressants, as well as three short courses of E.C.T., with only temporary improvement. An encouraging report (Regan, 1970) of the beneficial effect of haloperidol in obsessional states prompted a trial of haloperidol 5 mg. t.i.d. together with orphenadrine 100 mg. t.i.d. On the third day of treatment she developed torticollis (together with excessive salivation), and this was immediately controlled by 10 mg. of diazepam intravenously.

Case 3. R.B. was a 19-year-old single man admitted to hospital in a state of hypomania of sudden onset. He exhibited marked pressure of speech, and was restless, overactive and elated. Little change in his condition was noted on chlorpromazine 100 mg. t.i.d., and haloperidol 5 mg. t.i.d. was added after three days. Twenty-four hours later he developed widespread bizarre movements of all limbs and neck, which were hypertonic, and flexibilitas cerea could be demonstrated. There were also side to side movements of the jaw, with protrusion of tongue and marked salivation. While dystonia due to haloperidol was considered the most probable diagnosis, the possibility of catatonic schizophrenia was considered. Intravenous diazepam 10 mg. was followed by immediate relief of all bizarre movements, and there were no subsequent schizophrenic developments.

Discussion

Dystonic reactions to phenothiazines are common in psychiatry and occur not infrequently when these drugs are given, for example as antiemetics, to children and other patients. The most common way by far of treating these reactions is by anticholinergic drugs. These—in particular procyclidine, biperiden and benztropine—are usually effective. However, this is by no means always so, and patients have been described who have not responded satisfactorily even to intravenous use of these drugs (Christian and Paulson, 1960; Paulson, 1960; Waugh and Metts, 1960; Smith and Miller, 1961). Moreover, although psychiatrists and neurologists frequently use intravenous anticholinergics, other physicians have less experience with them. Diazepam, on the other hand, has the advantage of being widely used in many branches of medicine. It is, therefore, easily available and most doctors are familiar with its use.

We have found intravenous diazepam a reliable method of treatment of the various dystonic reactions described. Not only is the response rapid, but the patient feels only drowsy and does not fall asleep as he may when given sufficient barbiturate intravenously to control the dystonia. Diazepam has an advantage over the anti-parkinsonian drugs in the absence of side-effects, and in particular the absence of central effects which may cause an acute organic mental reaction. Diazepam has been widely used both orally and parenterally in tension states, premedication, muscular spasms and epilepsy (Gastaut *et al.*, 1965; Elian, 1969; Lavy and Assael, 1969) and it is considered to be a safe drug. The anxiolytic action of diazepam may also be important to the patient who suffers from a disturbing, frightening dystonic reaction.

The mechanism by which dystonic postures are produced is obscure. Pathological processes in the basal ganglia probably play a part. The response to anti-parkinsonian drugs suggests that there is excessive cholinergic activity, although this excess could of course be only relative (for example due to deficient dopaminergic activity). How diazepam acts on these processes it is not easy to speculate. It is possible that its action is a non-specific depression, similar to that of barbiturates albeit less generalized.

The effect of diazepam on other acute dystonias, such as oculogyric crises in patients with post-encephalitic parkinsonism, could perhaps shed some light on this problem.

Drug-induced dystonias are distressing, and immediate relief by *intravenous* diazepam is indicated. However, it will be interesting to see whether *oral* diazepam can be used for their

prevention, in the same way as it is used as an anticonvulsant (Elian, 1969).

Summary

Dystonic reactions appearing during treatment with phenothiazines or butyrophenones may take bizarre forms, posing diagnostic problems and sometimes endangering life. Many therapeutic measures have been suggested, but all are either unreliable, or slow-acting, or may confound the clinical picture.

Diazepam given intravenously was found to be effective in stopping immediately the various drug-induced dystonias. This safe agent seems to be the drug of choice in the diagnosis and treatment of this type of neuro-psychiatric emergency.

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