Persistent Parkinsonism Following Neuroleptanalgesia

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The expanding use over the last two decades of phenothiazine, thioxanthenes and butyrophenone drugs continues to underscore the neurologic complications associated with their use. The most common of these complications are extrapyramidal phenomena such as acute dystonias, akathisias, parkinsonism-like syndromes and the tardive dyskinesias. The extrapyramidal manifestations occur primarily as complications of psychiatric therapy, but recent innovations in the field of anesthesia, specifically dissociative analgesia or neuroleptanalgesia, have increased the population exposed to these agents.

Innovar, a compound of fentanyl and the butyrophenone derivative, droperidol, produces the neuroleptanalgesic state. The pharmacologic properties of these agents individually and in consort have received considerable attention. Various respiratory and cardiovascular side-effects have been reported, but extrapyramidal reactions, particularly rigidity and worsening of pre-existing parkinsonism, are rare and transient complications. The following report describes development of classic parkinsonism subsequent to the administration of Innovar to a previously healthy teenage girl.

REPORT OF A CASE

A 16-year-old Caucasian girl, a student and gymnast, was admitted to an outlying hospital in Houston, Texas, for surgical removal of impacted molars. At the time of admission she was asymptomatic, taking no medication, and general physical examination disclosed no abnormality. During the preoperative period, the patient was given promethazine, 25 mg, and meperidine hydrochloride, 50 mg, by intramuscular injection. Four impacted third molars were removed during general anesthesia with Innovar 3 ml, iv, and nitrous oxide inhalation. No complication occurred during or immediately following the procedure, which lasted 2 hours and 40 minutes.

The patient did not receive any medication postoperatively. Her course was unremarkable until the following day, when she complained of uncontrollable tremor of all four extremities, described as "intermittent resting tremor" by her physicians. Diplopia, which disappeared after a few hours, also developed. Results of examination were reported as otherwise normal. Treatment with diazepam and diphenhydramine for two days did not alleviate the tremorous condition. The third day, cog-wheel rigidity in both upper extremities developed, and the patient had a fine resting tremor in all limbs, aggravated by the antigravity position. Neurologic examination disclosed no other abnormality. Benzotropine (Cogentin), 2 mg, produced substantial alleviation of the tremor, lasting 4 to 6 hours, and subsequent oral therapy with this medication in doses fluctuating between 3 and 6 mg per day achieved some improvement of the patient's condition. On the seventeenth day, coincidental with an upper respiratory infection, tremor and rigidity worsened and appeared primarily localized to the right upper extremity. Benzotropine was increased to 8 mg per day, but the symptoms persisted. Because of refractoriness of her condition to this treatment, the patient was transferred to the Department of Neurology, Baylor College of Medicine.

Examination on admission disclosed mask-like facies, with poor facial expression and infrequent blinking. Marked bradykinesia with increased muscle tone in the upper extremities, mainly on the right, with cog-wheel rigidity of the shoulder, elbow and wrist, was apparent. The associated movements of gait in the right side were impaired. The patient had resting, intention, and positional tremor of the hands, more severe on the right, where the forearm and arm were also involved. Neurologic and physical examinations disclosed no other abnormality. Results of complete blood count, serum electrolyte and enzyme concentrations, ceruloplasmin levels and copper concentrations in urine and serum, cerebrospinal fluid, roentgenograms, EEG, EKG and brain scan were all normal.

Hospital Course. Benzotropine had decreased to 4 mg per day and, because the rigidity and tremor persisted, levodopa, 100 mg four times a day, alpha-methylidopa, 65 mg a day, and propranolol, 10 mg three times a day, were administered over the next 10 days. The neurologic symptoms subsided and the patient was discharged without medication six weeks after the beginning of her illness.

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DISCUSSION

Neurologic syndromes induced by phenothiazines, thioxanthenes, and butyrophenone drugs may manifest as acute dystonic reactions, akathisias, tardive dyskinesias or parkinsonism-like syndromes. The acute dystonias usually appear abruptly as bizarre spasms predominating in the head and neck muscles. Facial grimacing, torticolis, and difficulty with speech or swallowing occur frequently. Spasms of the external ocular muscles occur less often, persisting for minutes to hours. The dystonias usually appear 24 to 48 hours after drug exposure, predominate in the young, and putatively reflect a relationship of dose and individual sensitivity. Akathisia (the subjective feelings of restlessness) usually antedates observable motor restlessness. The tardive dyskinesias are generally recognized as complications of prolonged use. Lingual-facial buccal movements characterize this peculiar disorder, which has been found almost exclusively in patients under treatment with phenothiazines for psychotic disorders or "organic brain syndrome," but may also occur as an iatrogenic syndrome in non-psychotic patients.

Several studies evaluating experience with Innovar differ in the occurrences of isolated extrapyramidal reactions related to use of the drug. Mild akathisias, acute dystonias, and parkinsonism-like tremors have been reported to occur following administration of Innovar, but they are usually transitory and subside spontaneously. Infrequently, brief therapy with an anticholinergic drug of the type used in parkinsonism is necessary. The incidence of these extrapyramidal reactions is small (0.9 per cent, 0.21 per cent). The development of these phenomena has been attributed to the butyrophenone derivative, droperidol, contained in Innovar.

The mechanism by which certain drugs induce extrapyramidal syndromes is not completely understood. Theoretically, symptoms emerge due to imbalance of the cholinergic and dopaminergic systems within the extrapyramidal system. The abnormality produced by droperidol is probably a postsynaptic receptor block and not a result of dopamine depletion. Although the patient described in this report had an initial favorable response to the anticholinergic, benztropine, the symptoms returned later and worsened. Better results were obtained with levodopa combined with alpha-methyl dopa. This drug presumably as a decarboxylase inhibitor, antagonizing peripheral conversion of levodopa to dopamine, leaving more levodopa available for central utilization. This suggested to us the presence of competitive inhibition of dopamine in the striatum by droperidol, which has been indicated by results of experimental work with neuroleptics such as phenothiazines and haloperidol. Haloperidol, like droperidol, is a butyrophenone. Propranolol, a beta-adrenergic receptor blocker having favorable effects on certain types of tremors, was also administered.

This case illustrates a rare complication of general anesthesia with Innovar, presumably resulting from the effect in the dopaminergic systems of droperidol contained in the compound. The persistence of the parkinsonian symptoms and the ultimate response to levodopa, decarboxylase inhibition, and beta-adrenergic receptor blockers are interesting features of this case.

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REFERENCES

Nitrous Oxide and Pressures and Volumes of High- and Low-pressure Endotracheal-tube Cuffs in Intubated Patients

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Studies in vitro have demonstrated that nitrous oxide diffuses into the cuffs of endotracheal tubes and increases cuff volumes and pressures.1 This study was conducted to determine the effects of nitrous oxide on the volume and pressure of endotracheal tube cuffs in intubated patients.

METHODS

Eight commercially available 8.0-mm-ID endotracheal tubes were studied. Five of the tubes had high-residual-volume, low-pressure cuffs (Portex, Soft-seal; Foregger, Soft-cuff; American Hospital Supply, Hi-Low; Harris-Lake, Harlake and Shirley) and three had low-residual-volume, high-pressure cuffs (Portex; Foregger, Red Rubber; American Hospital Supply). Twenty tubes of each type were studied in 160 anesthetized women, 20–50 years of age, undergoing gynecologic, plastic, or general surgical procedures.

In every case the patient was premedicated, anesthesia was induced (sodium thiopental, 3–4 mg/kg), the patient was paralyzed (succinylcholine 1.5 mg/kg), and the trachea was intubated in the usual manner. Immediately after intubation, and before succinylcholine paralysis disappeared, the endotracheal tube cuff was filled with air until the trachea was just sealed. The volumes of gas in the cuff were then measured with a calibrated syringe and cuff pressures were measured with a calibrated standard pressure transducer or sphygmomanometer attached to the tip of the cuff catheter. Anesthesia was maintained with 60 per cent nitrous oxide, 38–40 per cent oxygen, and reactions after the use of Innovar® for ambulatory dental patients. Oral Surg 32:358–361, 1971


