Efficacy of a New Psychotropic Drug in Bronchoscopy

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For many years, bronchoscopy has been performed by most physicians with the use of sedation and a topical anesthetic. More recently there has been a trend toward the use of general anesthesia for this procedure in order to spare the patient an unpleasant experience. However, general anesthesia usually makes the procedure more drastic and more expensive. Many bronchoscopies, moreover, are now done for the purpose of treatment rather than diagnosis, and it is important to maintain the cough reflex in order to perform a satisfactory therapeutic aspiration of the bronchial tree. In our experience, such aspiration can be carried out better under topical anesthesia than is possible under general anesthetic. It would be advantageous, however, to find some means of reducing or even eliminating the dread and repugnance which many patients exhibit toward endoscopy.

The introduction of drugs with the specific action of reducing anxiety and emotional resistance has greatly improved methods of premedicating the surgical patient. Many authors have reported chlordiazepoxide (Librium)* as almost ideal for the purpose.1,2

In bronchoscopy we hope to obtain from a psychotropic drug three effects essential to success: relaxation, cooperation and intact cough reflex. A fourth effect is amnesia about the whole procedure. The patient undergoing bronchoscopy for the first time needs the assurance that he will probably remember nothing of his experience; and if the procedure must be repeated later, his previous amnesia is likely to insure acceptance. In this important respect, chlordiazepoxide was found wanting, as Brandt and associates' have also noted.

* Hoffmann-La Roche Inc., Nutley, New Jersey.

The first analog of this drug, diazepam (Valium)** was demonstrated in extensive clinical trials to resemble chlordiazepoxide in its high safety index, while exerting a more potent action on severely disturbed psychiatric patients and on those suffering somatic illness and pain.3,4,5 We instituted a study of this new agent in 201 private patients undergoing bronchoscopy. A double-blind method seemed unnecessary, since our routine was unchanged in all but one respect — the addition of diazepam to our premedication agents.

Materials and Methods
The series under study included 116 men and 85 women aged 14 to 80 years, of whom 101 were between 40 and 60 years of age. Many patients were admitted for bronchoscopic aspiration; in others the procedure was diagnostic — those with unexplained hemoptysis, abnormal x-ray films, possible carcinomas, etc. The largest diagnostic groups were: chronic bronchitis (70), pulmonary emphysema (25), bronchiectasis (20), possible carcinomas (20), pneumonitis or unresolved pneumonia (11), and suspected pulmonary tuberculosis (10).

All patients received 100 to 150 mg. of pentobarbital (Nembutal) orally 45 to 60 minutes prior to endoscopy. At the same time, they were given 50 to 100 mg. meperidine hydrochloride (Demerol) or 10 to 15 mg. morphine intramuscularly. The pharynx, soft palate and larynx were sprayed with 2½ or 5 per cent hexylcaine (Cyclaine). Tracheal and bronchial anesthesia were accomplished by instilling the anesthetic solution into the trachea by means of a laryngeal cannula. After a satisfactory topical anesthesia was obtained,
the patient was placed on the operating table and given an intravenous injection of diazepam. This was done slowly in 2.5 mg. increments while the patient was kept talking about his symptoms, his family or anything else that held his interest. A pause of 30 to 60 seconds between increments of injection allowed us to observe the effects before making subsequent injections. As soon as speech became slurred the patient was considered to have reached an optimal dose. A lateral nystagmus and sometimes slight blurring of vision were other indications noted, as well as "heavy eyelids."

The point of optimal sedation was usually reached at a dosage between 5 and 7.5 mg. (Table 1). The maximum dose used in this series was 10 mg., given to individuals who were large and heavy, or especially apprehensive. The minimum of 2 to 4 mg. proved sufficient in most elderly patients. However, there was no consistent correlation between the required dosage of diazepam and age, weight or amount of preoperative medication. However, it appeared that patients arriving in the operating room in a more than average state of sedation required less diazepam, possibly indicating an additive effect of diazepam to the barbiturate.

Onset of drug effect was within two to three minutes as a rule, and was never delayed beyond three minutes. Drug effect lasted 20 to 30 minutes in almost all patients and up to 60 minutes in a few. There was no pain at injection site; one patient reported mild discomfort. The symptom of thickened speech proved a reliable guide to dosage with a few exceptions (which were noted in retrospect). Only one patient was given a second dose of diazepam; this was a man aged 55 years who received 5 mg. stat and then was administered 3 mg. more before bronchoscopy. An occasional patient became unresponsive to commands, but after a delay of three to five minutes, again became responsive and the procedure was performed.

**Results**

As already noted, the four effects we hope to obtain from a psychotropic drug used in bronchoscopy are:

1. retention of cough reflex; 2. amnesia for the procedure; 3. cooperation, and 4. relaxation.

Of the 201 patients, only five responded poorly in all parameters; in one case bronchoscopy had to be deferred. Insufficient topical anesthesia was blamed for one failure, and inadequate diazepam dosage for the others.

Seven patients had uneven response: in five the cough reflex and amnesia were good, but cooperation and relaxation were poor to fair; in the other two it was felt that amnesia of the procedure, when the patients were questioned in their rooms after the day's schedule was completed, was not established.

Aside from these 12 patients, the diazepam action was considered good or excellent in all parameters. Thus, 189 (93.5 percent) of the series, went through bronchoscopy without excitement or resistance, coughed when directed, and forgot the whole experience subsequently. Aside from the five failures, there was no obtunding of the cough reflex, and amnesia was incomplete in only three. These two effects were considered the most essential to success in bronchoscopy; relaxation and cooperation were noted on the case reports only when they were conspicuously helpful to the procedure.

Often the relaxed and cooperative states induced by diazepam were determining

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**Table 1— Intravenous Dosage of Diazepam in 201 Bronchoscopies**

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Factors in a successful bronchoscopy. A woman aged 20 years with a diagnosis of chronic bronchitis was admitted in a state of marked anxiety, irritation and apprehension, showing every sign of emotional resistance. After administration of diazepam she became quiet, cooperative and appreciative of the treatment given her, ending with complete amnesia for the procedure. A man aged 44 years with hemoptysis had previously been impossible to bronchoscope, but this was accomplished easily on diazepam, also with subsequent amnesia.

Roughly 40 per cent of the series had mild side effects, chiefly muscle weakness, vertigo and slight blurring of vision. All of these effects were short lived and did not interfere with the procedure.

Summary and Conclusions

A series of 201 private patients bronchosoped for diagnostic or therapeutic reasons was administered the new compound diazepam (Valium) as adjunctive premedication aimed at reducing anxiety. Dosage was intravenous, at a level of 5 to 7.5 mg. for most patients. In appraising drug effects, the parameters of intact cough reflex, relaxation, cooperation and amnesia for the procedure were of paramount importance. Five showed poor response, seven others fair, and 189 (93.5 per cent) were rated good or excellent by all criteria.

The authors consider diazepam a promising drug for use in endoscopy. There was no serious complication and no evidence of respiratory depression or hypotension. This study was originally undertaken because of the muscle relaxing properties of diazepam discovered by other investigators. A certain amount of muscle relaxation was in fact obtained during endoscopy, facilitating the procedure. However, a more interesting effect of this drug was its amnesic action. In interrogating the patients several hours after endoscopy, the great majority remembered the administration of the topical anesthetic, but little or nothing of the following procedure.

Thus intravenous diazepam used in conjunction with preoperative sedation and topical anesthesia has removed the unpleasant effects to the patient of bronchoscopy and esophagoscopy, without producing any serious complication. It is our opinion that diazepam will prove to be valuable and helpful in endoscopy in the future.

Resumen

A grupo de 201 enfermos de clientela privada a quienes se hizo broncoscopia se adminis- tró el nuevo compuesto diazepam (Valium) como agregado para reducir la ansiedad. Se dio por vía intravenosa, de 5 a 7.5 mg. para la mayorí. Al valor sus efectos los parámetros de conservación de reflejo susígeno, relajamiento, cooperación y amnesia del procedimiento fueron los más importantes. Cinco enfermos tuvieron deficiente respuesta, siete aceptable y 189 (93.5 por ciento se estimaron como de buena o excelente respuesta desde todos puntos de vista.

Los autores consideran al diazepam una droga prometedora en la endoscopia. No hubo complicaciones serias ni evidencia de depresión respiratoria o hipotensión. Este estudio se inició al conocerse las propiedades musculorelajantes descubiertas por otros autores. Se obtuvo cierta re- lajación muscular durante la endoscopia, lo que facilitó el proceder. Sin embargo, un efecto más interesante de esta droga fue el amnésico. Al interrogar a los enfermos varias horas después de la endoscopia, la gran mayoría recordaron la ad- ministración del anestésico local tópico, pero poco o nada de lo que se hizo después.

Así que diazepam usado en combinación con la sedación preoperatoria, y anestesia local des- carató los efectos desagradables de la broncoscopia y de la esofagoscopy sin serias complicaciones y por tanto será valiosa en el futuro.

Zusammenfassung

Eine Serie von 201 Privatpatienten, die aus diagnostischen oder therapeutischen Gründen bronchoskopiert wurden, erhielten das neue Medikament Diazepam (Valium) als zusätzliche Prämedikation, dazu bestimmt, Angst- und Span- nungsgefühl zu verringern. Bei intravenöser Verabfolgung betrug die Dosierung in den meisten Fällen in Durchschnitt 5-7,5 mg. Bei der Bewer- tung von Arzneimittelnebenwirkungen waren die Hilfswerte des unbeeinflussten Hustenreflex, der völligen Entspannung, der Mitwirkung des Pa- tienten bei der Untersuchung und der Amnesie hinsichtlich des Eingriffes selbst von höchster Wichtigkeit. 5 Patienten reagierten nur wenig, 7 befriedigend und bei 189 (93,5%) war das Er-
gebhnis gut oder ausgezeichnet und zwar für alle erwähnten Kriterien.


Man kann also sagen, daß Diazepam auf intravenösem Wege und in Verbindung mit einer präoperativen Sedation und Lokalanästhesie die unerwünschten Nebenwirkungen für einen zu bronchoskopierenden Patienten zu geben ist. Dies gilt auch für die Oesophagoskopie, und es entstehen keine ernsthaften Komplikationen. Wir vertreten die Auffassung, daß das Diazepam sich als wertvoll und hilfreich in der Endoskopie zukünftig erweisen wird.

**References**


For reprints, please write Dr. Rogers, 1918 West Clinch, Knoxville.

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**GAS MIXTURES IN PNEUMONIA, ATELECTASIS, INFARCTION**

Seventy selected patients in whom diagnosis of pneumonitis, atelectasis or lung infarction was reasonably proved were examined by means of three serial roentgenographic studies: a) a preliminary film; b) an examination made after 10 to 15 minutes of inhalation of pure oxygen, 70 per cent helium-30 per cent oxygen, 80 per cent helium-20 per cent oxygen, and c) radiographs obtained 15 minutes after the second study, with the patient breathing room air. Radiographs obtained following the inhalation of an 80 per cent helium-20 per cent oxygen mixture demonstrated relatively increased radiolucency in certain of the eight cases of lung infarction during the first 24 to 72 hours of their evolution. These observations raise but do not establish the possibility that this approach may yield findings helpful in making an early diagnosis.

**ANGIOTENSION-INFUSION TEST**

Patients with functionally significant renovascular hypertension were more resistant to the pressor effect of synthetic angiotensin II than those with other types of nonmalignant hypertension. The pressor response is determined by infusion of progressively increasing amounts of angiotensin intravenously until the diastolic blood pressure rises 30 mm. of mercury. Whereas patients with renovascular hypertension require more than 6.5 millimicrogram per kg. body weight per minute, almost all patients with other types of nonmalignant hypertension require less than 5.0 millimicrogram per kg. per minute for a pressor response. On the basis of initial results, the infusion of a single dose of angiotensin, 4 millimicrogram per kg. per minute, over a five-minute interval has been used as screening test. The test is invalidated by the presence of malignant hypertension, salt-retaining states and depletion of plasma volume.

**References**