NISENTIL IN CYSTOSCOPY*

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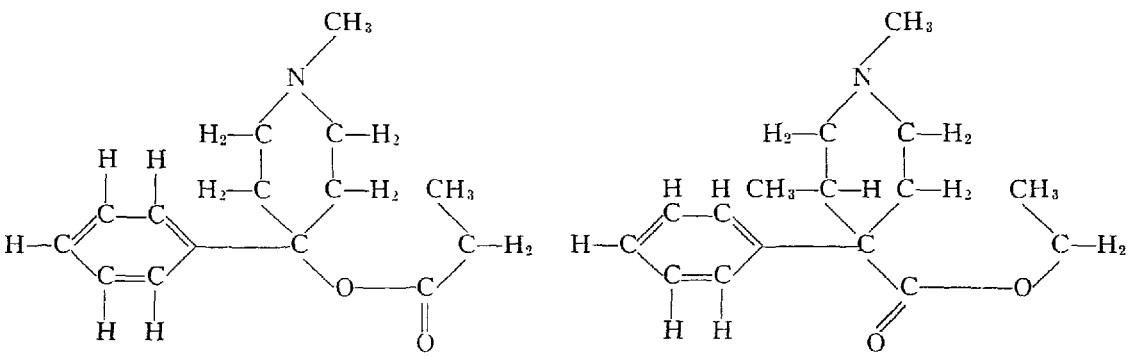
WITH the synthesis of Nisentil in 1947 by Ziering and Lee (1), and the study of its pharmacological properties by Holland and Gross (2), and Randall and Lehmann (3), many different clinical uses have been prescribed for this drug The new analgesic drug has been advocated for the relief of pain, for analgesia in obstetrics (4, 5, 6, 8), for preanaesthetic medication, and for short surgical procedures including cystoscopy (7). It is the purpose of this study to assess the value of Nisentil as an alagesic agent for cystoscopy and retrograde pyelography.

Before proceeding with our study it would be profitable to review the pharmacological properties of Nisentil. The drug is a synthetic homalogue of Demerol and structurally they are closely related, both having basically a 4-phenyl piperidine structure This is shown in Figure 1



Demerol Nisentil

FIGURE 1

Nisentil is an analgesic which is more potent than Demerol but less potent than morphine (the effective dose is between 30 and 60 mg.). Its sedating effect is moderate, and also lies between those of morphine and Demerol The respiratory centre is depressed by the drug especially in the presence of other opiates or barbiturates There is little effect on the cardiovascular system with only slight fluctuation of blood pressure and pulse rate Decrease of the respiratory minute volume is through the depression of the respiratory centre. The effect is mainly on the rate, especially with larger doses. The onset of action is rapid, from 1 to 5 minutes (7) when administered intravenously and 3 to 15 minutes (6) intramuscularly. The duration of action is brief, varying from 1½ to 2 hours

METHOD

Clinical observations on the analgesic effects of Nisentil were made on patients undergoing cystoscopy and pyelography. The subjects comprised a random selec-

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tion of patients who were admitted and discharged the same day from the hospital, outpatients, and regular hospital inpatients as illustrated in Table I. There were 34 per cent outpatients and 66 per cent inpatients, their ages ranging

TABLE I

NISENTIL FOR CYSTOSCOPY

	Nisentil	Nisentil–Pent	Nisentil–Pentothal Nitrous Oxide	Total
Cases	76	38	21	135
Per cent	56	27	17	100

	Cases	Per Cent	Premedication with Opiates	Cases	Per Cent
Inpatients	88	66	Premedicated	91	68
Outpatients	47	34	Not premedicated	44	32
Total	135	100	Total	135	100

from 12 to 83 years of age. The majority of the patients (68 per cent) were premedicated with morphine or Demerol plus atropine or hyoscine and the remainder (32 per cent) with only a belladonna drug Premedications were given one hour before the anaesthetic procedure

Nisentil was administered intravenously immediately prior to the preparation of the patient for surgery so that there was a lapse of approximately 3 to 5 minutes before the insertion of the cystoscope The effectiveness of the analgesia was judged by both subjective sensations of the patient and objective findings of discomfort such as movements, grimaces, moaning, etc. Dosage of Nisentil ranged from 30 to 60 mg; repeated small doses of 10 mg. may be injected when initial analgesia is found to be inadequate.

In our second group, Nisentil was administered intravenously as above in doses of 30 to 40 mg before the preparation of the patient. Pentothal or Surital was then injected in small hypnotic doses just before the insertion of the cystoscope. Usually no further injection of Pentothal was required after the initial insertion of the cystoscope.

Finally, in the third group, Nisentil was combined with Pentothal and Nitrous Oxide, which was administered throughout the procedure so that the patient was completely anaesthetized for the duration of the examination.

RESULTS

Of the 30 male and 46 female cases (Table II) of cystoscopy and pyelography handled with Nisentil alone, 66 cases, or 87 per cent, were completed satisfactorily without other supplementary agents. Nisentil afforded complete analgesia with no discomfort in 42 per cent of the cases in which there were 30 per cent of

TABLE II

DEGREE OF ANALGESIA WITH NISENTIL

	Satisfactory								Unsatisfactory	
	No Discomfort		Slight Discomfort		Moderate Discomfort		Total		Total	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Male	9	30	13	44	5	13	26	87	4	13
Female	24	52	15	32	1	2	40	86	6	14
Total	33	42	28	37	6	8	66	87	10	13

Side reaction	Cases	Per cent
Dizziness	4	
Nausea and vomiting	1	
Cheyne-Stokes respirations	1	
Total	6	8

the male and 52 per cent of the female cases In 37 per cent of the cases there was slight discomfort, among these were 44 per cent of the males and 32 per cent of the females. In 8 per cent of the cases there was moderate discomfort initially, but this was relieved by larger doses of Nisentil In 13 per cent of the cases Nisentil alone was not sufficient and other supplementary agents were required to complete the cystoscopy.

The drug did not show any marked effect on the cardiovascular system; the blood pressure and pulse remained constant even in hypertensive subjects. However, respiration was markedly depressed, chiefly through a decrease in rate of respiration which may drop to 6 per minute for a brief period This depression was greater with increasing amounts of Nisentil and with the presence of opiates Sedation was variable Side reactions appeared in 6 cases or 8 per cent. these included dizziness in 4, nausea and vomiting in 1, and Cheyne-Stokes respiration in 1. The incidence of side reaction was seen particularly in unpremedicated individuals.

Nisentil and Pentothal or Surital were administered to 38 cases in the series Pentothal was given chiefly at the commencement of the procedure for the insertion of the cystoscope, subsequently the patient was drowsy or awake while the pyelograms were being taken. The amount of Pentothal used during the procedure was significantly less than in cases done with Pentothal alone (Table III). The average dose of Pentothal required with Nisentil was 260 mg. in males and 117 mg. in females, as compared to the amounts with Pentothal alone which were 711 mg. for males and 620 mg. for females. Patients anaesthetized with Nisentil and Pentothal were awake or responded to commands while those given

TABLE III

DOSAGE OF PENTOTHAL FOR CYSTOSCOPY

	Pentothal	
	Range	Average
Male	400 to 1200 mg	711 mg
Female	400 to 1000 mg	620 mg

	Nisentil–Pentothal	
	Range	Average
Male	50 to 675 mg	260 mg
Female	50 to 225 mg	117 mg

Pentothal alone were unconscious or slightly reactive at the end of the examination

The main side reaction of this method was the marked depression of respiration when Nisentil was combined with Pentothal Patients may have very slow respiration or complete apnoea with large doses or with rapid injection of Pentothal. If apnoea occurs gentle inflation of the lungs with oxygen will restore respiration in a few minutes

In the third group of cases, where the combination of Nisentil, Pentothal and Nitrous Oxide was used, patients remained completely anaesthetized throughout the procedure Here again the amount of Pentothal used was markedly reduced Patients returned to consciousness rapidly at the end of the procedure The chief side reaction here was again a brief period of respiratory depression

DISCUSSION

The usefulness of Nisentil in cystoscopy has been assessed in this study It has been found that successful cystoscopy and pyelography were carried out in 87 per cent of the cases without other supplementary agents The drug has the property of brief duration of action so that the narcosis soon wears off after the examination With this method the patient remains drowsy but awake so that he is able to co-operate and the pyelograms can be taken without any movement of the diaphragm. The respiratory depression is readily coped with by administering oxygen to the patient by mask Oxygen should be given if there are any signs of respiratory depression especially in older individuals. Successful cystoscopy and pyelography can be carried out with this technique both in hospital and office practice if complete analgesia is not anticipated by the patient, since approximately two-fifths of the subjects may have slight discomfort from instrumentation Nisentil alone is most suitable for the examination of female patients since 52 per cent suffered no pain. This is due to the fact that the female urethral is short and straight so that less analgesia is required.

Nisentil alone is not satisfactory if complete pain relief is contemplated by the patient because only 43 per cent (30 per cent male and 52 per cent female) have complete analgesia.

Nisentil in combination with Pentothal offers an alternative which is useful because it eliminates the discomfort of the insertion of the cystoscope and yet allows the patient to be sufficiently awake to co-operate during the pyelography. The initial injection of Pentothal is sufficient to relieve the initial discomfort while the Nisentil provides adequate analgesia when the cystoscope or ureteral catheters remain in the urethra. When Nisentil and Pentothal are used together competent personnel must be available to contend with the respiratory depression and apnoea which may occur. Usually a brief period of ventilation of the lungs with oxygen will restore adequate respiration. The advantage of the technique is that the amount of Pentothal is reduced significantly so that there are no prolonged after effects.

The combination of Nisentil, Pentothal, and Nitrous Oxide gives complete anaesthesia throughout the examination. The emergence from anaesthesia is rapid The patient is usually awake before leaving the operating room. Here again apnoea may occur so that a competent anaesthesiologist should be present.

There were side reactions in 8 per cent of the cases, most of which were of minor nature Dizziness, which was most common, was not seen in cases where there had been premedication with Demerol or morphine. Thus premedication not only reduces the incidence of side reactions but also reduces the anxiety of the patient, which is the prime purpose of the preoperative sedation. Finally, premedication reduces the amount of anaesthetic agent required during the anaesthetic.

Cystoscopy was used as a means to assess the analgesic action of Nisentil. Instrumentation of the urethra does not present a universally similar condition since there is a great variation between the male and female urethra The female urethra is short and straight thereby requiring less analgesia. Even in the male urethra there is a wide variation in the degree of analgesia needed; obstruction to the bladder neck by the prostrate gland is common so that severe pain may be inflicted when the cystoscope is forced through the tight bladder neck. For these reasons we have found that there is a wide variation in the dosage of drugs required and the results produced by the drugs. Nisentil has been found to be a potent short-acting analgesic drug with marked depressing effect on respiration

Summary

We have presented the results of a study of the analgesic effects of Nisentil in 135 urological cases The cases were divided into three groups in which Nisentil was used alone, in combination with Pentothal or Surital, and in combination with Pentothal and Nitrous Oxide Successful cystoscopy was carried out in 87 per cent of the cases where Nisentil was the sole agent When Nisentil was combined with Pentothal the amount of the latter drug was significantly reduced. The side reactions and the limitations of the method are discussed. As with other potent analgesic agents, Nisentil had a marked depressing action on the respiration.

RÉSUMÉ

L'auteur présente les conclusions qu'il a tirées de l'étude des effets analgésiques du Nisentil dans 135 examens cystoscopiques.

Les cas furent divisés en trois groupes . le Nisentil étant utilisé seul, ou bien avec Pentothal ou Surital, ou encore, avec Pentothal et Protoxyde d'azote. Employé seul, le Nisentil permit une cystoscopie facile dans 87 pour cent des cas. Combiné au Pentothal, il fut possible de reduire de façon significative, la dose de ce dernier. Les réactions secondaires furent les étourdissements (4 cas), les nausées et vomissements (1 cas) et la respiration de Cheyne-Stokes (1 cas) Comme tous les autres analgésiques puissants, le Nisentil produisit une dépression marquée de la respiration

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