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CLINICAL EXPERIENCE WITH A NEW ULTRA-SHORT-ACTING THIOBARBITURATE

H. GRANT-WHYTE, F.F.A.R.C.S. (ENG.), D.A.

Durban

Barbital was prepared by Fischer and von Meiring in 1905, and phenobarbital by Horlein in 1911; and in 1916 Schonle began to prepare the higher-molecular-weight derivatives. In 1930 Nembutal marked the beginning of the use of intravenous barbiturates, and Evipan sodium followed in 1932. In 1934 Sodium pentothal (thiopentone) was introduced by Lundy and Tovell at the Mayo Clinic.

It was stated by A. J. Clark in 1937 that the number of possible barbiturate homologues, none containing more than 6 carbon atoms in a side-chain, was in the neighbourhood of 1,225; today 100 have been prepared and used.

In anaesthesia, barbituric acid and its salts and derivatives are generically known as barbiturates. The most useful of them have been the ultra-short-acting group, which are characterized by rapidity of induction and pronounced intense hypnotic action of brief duration, followed by mild hypnosis or heavy sedation. This group have been useful for abolition of consciousness during surgical procedures. The barbiturates in this group are in the main 'thio' or sulphur containing; they are described as ultra-short-acting because of their rapid disappearance in the body. Detoxification takes place by the action of the liver, muscle tissue and the blood, possibly through enzyme action.

Constant search for new and innocuous ultra-short-acting barbiturates has resulted in the synthesis of a new thiobarbiturate—the sodium salt of methyl-thio-ethyl 2 pentyl-thiobarbituric acid, Neraval sodium (Sch. 3132), also known as Thiogenal. This drug is of particular interest because of the presence of the methyl-thio-ethyl radicle, which is present in methionine—an essential amino acid which has itself a detoxifying action.

SERIES OF CASES REPORTED

Neraval sodium has been used in 80 unselected cases by intermittent intravenous injection of aqueous solution of 5% concentration; all cases except dental extractions were supplemented with nitrous oxide and oxygen mixture 50 : 50. Muscle relaxants, long-acting or short-acting, were used when surgical procedures demanded their use. Pre-anaesthetic medication with Omnopon, 1/6th to 1/3rd gr., and scopolamine, 1/300th to 1/150th gr., was administered 1¼ hours before operation, except for dental extractions, when no preliminary narcotic was administered because they were carried out in dental chambers.

The table below shows an analysis of cases by type of surgery, age range, and dosage of Neraval sodium 5% and of long-acting relaxant (Laudolissin- Laudexin) and/or short-acting succinylcholine chloride (Scoline) when these were employed.

Neraval sodium is a crystalline substance, yellowish in colour and dissolving slowly in distilled water, forming a solution which has a sulphurous odour. A 2·5% solution has a pH of 9·42, a 5% solution 9·32 (2·5% Sodium pentothal has a pH of 10·5). Deterioration of solutions is said to occur in much the same way as with solutions of other thiobarbiturates, although 40 c.c. of a 5% solution of Neraval sodium was kept 2 days in a refrigerator and exhibited no loss of potency when used subsequently.

DOSAGE AND ADMINISTRATION OF NERAVAL SODIUM 5%

The average human dose for the induction of sleep is in the region of 0·01 g. per kg. of body-weight, and the same precautions were taken with this drug as with other barbiturates.

A slow rate of intravenous administration is advisable, and was in fact practised because it was found in the first few cases that too rapid injection resulted in coughing due to laryngeal irritation. The practice subsequently was to administer 1 c.c. as a test dose and subsequently fractional doses of 3 c.c. Sleep was induced with 6-15 c.c. of 5% solution.

Larger repeat doses had to be administered than

EIGHTY SURGICAL PROCEDURES UNDER NERAVAL NARCOSIS

Type of Surgery	*No. of Cases*	*Age Range (Years)*	*Average Dose of Neraval Sodium 5% (g.)*	*Relaxant Drug*
1. *Dental Extractions*	6	15-18	0·5-1·5	
2. *Gynaecological*	18	28-50	1·0-2·0	Laudolissin 30-60 mg. Nil
Ventrosuspension and operations on adnexa Insertion of radium Dilation of cervix Dilation of vagina Vaginal hysterectomy Opening pelvic abscess				
3. *Urological*	17	30-84	1·5-3·5	Laudolissin 30-60 mg.
Cystoscopy Suprapubic cystotomy Suprapubic prostatectomy Retrograde pyelogram with extensive cystodiathermy Urethral dilation				
4. *General Surgery*	29	18-60	1·5-3·5	With and without Laudolissin 30-60 mg. or Scoline 70-100 mg.
Appendectomy Herniorrhaphies, direct, indirect, post-operative and ventral Tumours of breast, simple and malignant Mobilization of colostomy and closure Sigmoidoscopy Haemorrhoidectomy				
5. *Orthopaedic*	6	24-55	1·0-1·5	Scoline 70-100 mg.
6. *Thoracic*	4	28-35	1·5-2·0	Laudolissin 30-60 mg.

would have been the case if Sodium pentothal had been used, and there was no difference between the two drugs as far as the production of hypotension was concerned, the fall of blood pressure being more pronounced in hypertensive patients than in normotensive.

Extravenous injection of Neraval sodium in 2 cases in the series produced the usual discomfort experienced with Sodium pentothal, but the clinical impression was that Neraval sodium was less irritating to the endothelium of the veins, and led to less 'hardening' of the vein post-operatively. The reason for this is possibly the lower pH of Neraval sodium, resulting in less irritation of the endothelium and less tendency for the vein to thrombose.

Poor-risk octogenarians tolerated the drug extremely well. One of these oldsters received 3·5 g. of Neraval sodium over a period of 2½ hours and was awake within 15 minutes of leaving the operating theatre.

Laryngospasm was almost negligible in the series of cases. There was slight evidence of it in a few cases where the drug was administered with injudicious rapidity, but even in these there was no indication to use relaxant to alleviate the spasm.

SUMMARY

1. A brief clinical report is submitted on the use of Neraval sodium (Sch. 3132) in 80 unselected cases embracing a wide range of surgery.

2. Dosage and administration of Neraval sodium is discussed.

3. Beyond slight laryngospasm in 3 cases, and slight vein reaction in 2 other cases, there were no other untoward effects in the nature of severe respiratory depression or severe hypotension resulting from accumulation of the drug.

4. 'Waking up' time is markedly shorter than with other barbiturates, which is of great advantage to the patient, nursing staff and surgeon.

5. In conclusion, Neraval sodium has a definite use for brief surgical procedures; its use is free from unpleasant after-effects; and its outstanding quality is that it allows of rapid awakening after small or large doses.

I would like to express my thanks to the Schering Corporation, Bloomfield, New Jersey, USA, for supplying me with Neraval sodium for clinical trial.