COMPARATIVE HYPNOSIS PRODUCED BY METHITURAL (NERAVAL) AND THIOPENTAL

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AN INTRAVENOUS barbiturate with a shorter duration of action than thiopental would be useful in the practice of anesthesiology. Several reports (1, 2, 3) have appeared indicating that methitural sodium* produces a more evanescent hypnosis than does thiopental. Reifferscheid and Dietmann (4), using subjects serving as their own controls, reported that the duration of sleep following methitural was two-thirds that of thiopental. However, O'Herlihy, Nishimura, Little and Tovell (5) and Gale (6) have presented data suggesting that hypnosis following methitural and thiopental is of similar duration. Their results are not completely acceptable because narcotics were used for preanesthetic medication and the identity of the drugs under study was known. The following investigation was undertaken to obtain more definitive information on the duration of anesthesia produced by methitural as compared to thiopental.

METHOD

Data were obtained from one hundred and nine studies on 24 patients awaiting electroshock therapy (table 1). No preanesthetic medication was given. The decision was made to use equipotent concentrations and doses of the two drugs. A preliminary trial comparing the effects of various doses of methitural (Neraval) suggested that this drug was about one half as potent as thiopental; therefore, solutions containing either methitural (5 per cent) or thiopental (2.5 per cent) were prepared and labelled by number. The anesthetist was unaware of the identity of the drug being used. The agents were injected into the vein rapidly until the patient would not respond to a command. The volume of solution necessary to reach this end point was recorded. The patient was ordered to speak every 15 seconds until he awoke sufficiently to answer. The duration of sleep was measured with a stopwatch. Blood pressure and pulse rate were recorded before and within 30 seconds after onset of sleep. No other physical stimuli were permitted. Side effects attributed to the barbiturate were noted. Data on sleeping time, blood pressure and pulse rate changes were

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* Methitural (Neraval) sodium kindly supplied by Schering Corporation, Bloomfield, New Jersey.

TABLE 1

COMPARISON OF HYPNOSIS PRODUCED BY METHITURAL AND THIOPENTAL

Patient*	Methitural				Thiopental			
	Number Tests	Average Inject Time (seconds)	Average Dose (mg.)	Average Sleep Time (seconds)	Number Tests	Average Inject Time (seconds)	Average Dose (mg.)	Average Sleep Time (seconds)
A. B., 63 WF 59 88*	1	90	225	45	0	—	—	—
M. B. 67 WF 62 110	4	45.7	250	91.4	1	105	125	125
I. V. 60 WF 60 131	1	72	350	63	0	—	—	—
E. C., 50 WF 65 140	2	59.5	350	97.5	5	56.3	190	110.6
M. F., 43 WF 62 145	2	51	362.5	136.5	0	—	—	—
R. F. 51 WM 65 123	0	—	—	—	4	35.7	206.3	101.5
M. Fr., 53 WF 61 126	2	62	325	33	3	43.3	170.8	80
G. H., 46 WM 70 150	1	34	250	46	1	36	137.5	99
C. H., 60 WF 66 150	4	33.5	293.8	146	3	43.3	150	112.5
C. Ho., 73 WF 63 125	1	37	200	143	2	32	137.5	233
B. J., 67 WF 65 138	3	76.7	466.7	90	6	71.7	238.8	44.2
L. L., 68 WF 65 144	1	30	300	310	2	67.5	158.8	199
F. L., 65 WM 70 157	2	61	375	215	0	—	—	—
M. M., 68 WF 63 157	2	39.5	275	168	1	90	150	90
M. O., 66 WF 59 186	0	—	—	—	7	54.5	160.5	81.7
W. O., 56 WM 66 160	4	105	431.3	93.8	4	70.5	237.5	104.5
H. O., 67 WM 64 130	4	34.8	318.8	191.5	0	—	—	—
E. R. 72 WF 63 122	2	35	262.5	237.5	0	—	—	—
L. R., 61 WM 68 140	6	33	283.5	240	0	—	—	—
O. S., 51 WF 63 103	1	45	250	150	3	60	191.7	118.3
N. S., 62 WF 66 169	4	32.5	293.3	55	3	40	150	42.3
E. S., 37 WF 62 110	1	42	300	78	2	33.5	150	161.5
W. S., 45 WM 72 200	5	74	440	70.6	6	61.7	196	44.2
M. V., 55 WF 64 115	2	95	575	97.5	1	27	150	103
Mean		54.0	326	127.0		54.6	170.7	109
Standard deviation		22.7	—	73†		21.6	—	51.1†

* Initials, age, color, sex, height in inches, weight in pounds.
† Variance is not significantly different ($F = 1.95$).

analyzed for significant differences with t ratios, while a comparison of the incidence of side effects was made using the Chi square test.

Following the completion of the above procedure, the patient was reanesthetized with the same barbiturate, succinylcholine was injected intravenously, and electroshock therapy carried out. No data for the second period of anesthetization are included in this report.

Results

The time required for injection, dose used for hypnosis, and sleeping times are listed in table 1. The mean rates of injection for the two barbiturates were almost identical. The mean dose of methitural was 326 mg. and thiopental 170.7 mg. The average sleeping time after methitural was 127 seconds, after thiopental 109 seconds. The difference between the sleeping times of the two drugs was not statistically significant.

The pulse rate was not appreciably altered after either drug, but the systolic and diastolic blood pressures declined significantly ($P < .01$) (table 2). The average decrease in blood pressure after methitural was no greater than after thiopental.

TABLE 2

Blood Pressure Changes

Patient	Methitural			Thiopental		
	Number Tests	Before	After	Number Tests	Before	After
M. B.	4	138/77.5	102/51	1	130/64	102/52
M. Fr.	2	197.5/89	162/59	3	183/84.7	173.3/68.3
G. H.	1	196/65	128/50	1	200/100	134/74
C. H.	4	165/87.5	133/76	3	170.7/96.7	161.3/86
C. Ho.	1	120/70	122/78	2	127/75	111/64.5
L. L.	1	170/90	110/70	2	155/85	115/58
L. R.	6	127/76.5	101.5/59	0	—	—
N. S.	4	198.5/105	175/95	3	198/100	172/96
E. S.	1	120/76	96/60	2	110/71	99/59
W. S.	1	142/78	118/64	1	140/78	134/70
Mean change systolic blood pressure		-32.7 ± 19.7*			-23.6 ± 19.4*	
Mean change diastolic blood pressure		-15.3 ± 9.17*			-14.1 ± 7.8*	

* Standard deviation.

The principal undesirable side effects noted were coughing and hiccoughing (table 3). These were more frequent after methitural ($P < .05$), but led to no difficulties in the management of the patients. Neither laryngospasm nor complaints of burning in the vein were observed.

Discussion

We observed no significant difference in the duration of hypnosis produced by methitural or thiopental when equipotent concentrations and doses were used. Our results are, therefore, similar to those of Gale (6) and O'Herlihy, Nishimura, Little and Tovell (5). The slightly longer period of hypnosis noted after methitural may be an indication that our patients received relatively larger doses of methitural because of the use of a comparatively stronger solution of methitural. If the potency of methitural were somewhat greater than one-half that of thiopental, our study might be biased in favor of thiopental. This bias would be considerably less than in the studies of Reifferscheid and Dietmann (4), where equal concentrations of the drugs were used. Random selection of unknown solutions minimized this theoretical bias.

TABLE 3

Side Effects After Thiobarbiturates

Side Effect	Methitural (55)	Thiopental (54)
Cough	16 (29.1%)	7 (13%)
Hiccough	5 (9.1%)	1 (1.8%)
Twitch	1 (1.8%)	0
Thrombosis vein	1 (1.8%)	1 (1.8%)
Several together	3 (5.5%)	0
No side effect	35 (63.7%)	45 (83.3%)

It is possible that methitural does produce a more evanescent hypnosis than does thiopental, as has been claimed, and yet such advantage not be apparent in a study of this type. Blake and Perlman (7) have shown in animals that methitural is destroyed more rapidly than thiopental. If larger doses of the drugs were given, or if the period of administration were lengthened, a difference in the rate of metabolism might cause one drug to produce a more transient hypnosis. Irwin, Stagg, Dunbar and Govier (8) support this hypothesis with data showing that animals awaken more rapidly after methitural than after thiopental when large doses of the drugs were given. While patients do not awaken more quickly after small doses of methitural, they might do so after larger doses given over a prolonged period.

Side effects of methitural have been reported by many authors (1, 3, 5, 6, 9, 10). Although we observed coughing and hiccoughing more freqeuntly with this drug than with thiopental, these complications seemed harmless and stopped promptly with awakening.

Summary

One hundred and nine studies on 24 patients revealed no significant difference in the duration of hypnosis produced by small equipotent doses of methitural and thiopental. There was a comparable decrease in blood pressure with no significant pulse rate change after either

drug. Side effects (coughing and hiccoughing) were more common after methitural.

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