BUTHALITONE SODIUM ANAESTHESIA: DRUG CONSUMPTION AND SERUM PROTEIN STUDIES*

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AT THE TIME of their introduction, the early thiobarbiturates, derivatives of barbituric acid, appropriately deserved the designation of "ultra-short-acting" anaesthetics. Nevertheless, for office, dental or out-patient interventions, their effect still lasts longer than desirable. They also fall short of ideal by increasing vagal irritability and producing central and myocardial depression.

Weese and Koss (1) in introducing buthalitone sodium (Baytinal), a new thiobarbiturate, claimed that this agent had a shorter action and produced less respiratory depression. Extensive clinical trials in Europe (2-14) tend to confirm these views, but American experience with the drug is so far limited

Buthalitone sodium is the sodium salt of 5,5-allyl-(2'-methyl-propyl)-thiobarbituric acid. It is known in Great Britain at "Transithal" and on the European continent as "Baytinal"

We recently had the opportunity to use buthalitone sodium and we report here our findings

MATERIAL AND METHODS

Thirty-seven patients undergoing uterine curettage were the subjects of our study. The material was selected only in so far that patients with recent massive haemorrhage or marked debility were excluded from the trials. All subjects received routine premedication and buthalitone sodium was administered in a 5 per cent solution, usually through the subclavian vein (15). As soon as the eyelid reflex disappeared, high flow nitrous oxide (3 l) was administered by mask and respirations were vigorously assisted or controlled. Supplementary buthalitone sodium was given as necessary and the time of administration recorded. At the end of the intervention, note was made of the time when the subjects reacted to a standard stimulus, pinching of the trapezius muscle. The duration of anaesthesia or anaesthesia time was defined as the interval between the initial administration and the reaction to stimuli. The time when the patients were first able to correctly state their age was also noted.

From 23 of the 37 patients blood samples were taken immediately prior to induction and at the end of the procedure. Haematocrit, serum protein and protein distribution were determined on every sample, using standard clinical laboratory techniques of Wintrobe, nephelometry and filter paper electrophoresis respectively. The filter paper strips were evaluated with a semi-automatic scanning device (Spinco Analytron).

Earlier data from 24 curettages, where anaesthesia was performed by the same

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anaesthetist using an identical technique but with thiopentone as the intravenous agent, served as a basis for comparison in the drug consumption studies.

RESULTS

The consumption of buthalitone sodium as compared with that of thiopentone is given in Table I. Measures of recovery from anaesthesia are shown in Table II. In Table III are presented the serum protein and haematocrit values before and after anaesthesia. The statistical data relevant to protein changes and to the

TABLE I
DRUG CONSUMPTION FOR CURETTAGE IN PREMEDICATED PATIENTS
(using buthalitone B, 37 cases, or thiopentone T, 24 cases)

	B		T		V_{σ}		σ_M		t
	M	σ	M	σ	B (%)	T (%)	B	T	
Age (years)	37	± 13	37	± 12	35	32	2.1	2.4	
Weight (lb)	129	± 23	133	± 25	18	19	3.8	5.3	
Anaesthesia time (min)	22	± 8	26	± 8	36	30	1.3	1.6	1.94
Thicbarbiturate (mg)	652	± 269	415	± 164	41	40	42.5	34.1	4.3
Mg /lbs	5.1	± 2.0	3.2	± 1.3	39	41	0.33	0.28	4.4
Mg /min	30.1	± 15.6	16.8	± 8.6	52	51	2.56	1.79	5.5
Mg /lbs /min	0.23	± 0.12	0.13	± 0.07	52	54	0.0020	0.0014	42.0

TABLE II
RATE OF RECOVERY FROM BUTHALITONE SODIUM

	M	σ
Anaesthesia time (from initial administration to reaction to stimuli)	22.0	± 8.0 min
Duration of final dose (from last administration to reaction to stimuli)	9.4	± 4.3 min
Reaction time (from end of surgery to reaction to stimuli)	2.3	± 1.3 min
Answering time (from end of surgery to stating age)	6.0	± 4.2 min

TABLE III
SERUM PROTEIN AND HAEMATOCRIT VALUES, STANDARD ERRORS (σ) AND COEFFICIENTS OF VARIATION (V_{σ}) BEFORE AND AFTER BUTHALITONE Na ANAESTHESIA
(23 cases)

	Before			After		
	M	σ	V_{σ} (%)	M	σ	V_{σ} (%)
Haematocrit (%)	39.3	± 3.7	9	39.0	± 3.7	9
Serum protein (gm /l)	64.6	± 7.5	12	62.7	± 7.0	11
Albumin	33.3	± 6.5	19	32.1	± 4.3	13
α_1	2.8	± 0.7	25	3.0	± 0.6	20
α_2	6.9	± 1.3	19	6.9	± 1.7	25
β	9.6	± 1.9	20	9.2	± 1.8	20
γ	11.9	± 2.5	21	11.5	± 2.1	18

TABLE IV
STATISTICAL CHARACTERISTICS OF SERUM PROTEIN AND HAEMATOCRIT CHANGES
FOLLOWING BUTHALITONE ANAESTHESIA
(23 cases)

	B	A	Δ	σ_M	t	Δ'	$\sigma_{M'}$
	(preop)	(postop)	(B-A)	$\sqrt{\frac{N\sum x^2 - (\sum x)^2}{N^2(N-1)}}$	$\frac{\Delta}{\sigma_M}$	$\frac{A}{B} \times 100$	$\frac{\Delta'}{t}$
Haematocrit (H)	39.3%	39.0%	0.3%	0.091	3.30	1.0	0.30
	gm/L	gm/L	gm/L				
Protein (P)	64.6	62.7	1.9	0.502	3.00	-3.0	0.79
Albumin (A)	33.4	32.1	1.3	0.396	3.23	-4.0	1.22
α_1	2.8	3.0	-0.2	0.092	2.17	+7.1	3.27
α_2	6.9	6.9		0.119	0.17	-0.4	2.35
β	9.6	9.2	0.4	0.182	2.20	-4.7	2.14
γ	11.9	11.5	0.4	0.229	1.75	-3.0	1.71

Statistical significance (t) of the variations between the different protein fractions (at P 0.05 for 23 samples, $t = 2.07$)

A- α_1	3.18					
A- α_2	1.29	α_1 - α_2	1.79			
A- β	0.78	α_1 - β	3.00	α_2 - β	1.33	
A- γ	0.48	α_1 - γ	2.74	α_2 - γ	0.84	β - γ 0.62

significance of variations among the individual protein fractions are tabulated in Table IV.

Percentage changes of the protein fractions and the standard deviations of the mean are plotted in Figure 1.

DISCUSSION

As seen in Table I, buthalitone sodium is indeed a shorter-acting agent than other thiobarbiturates now in common use. The drug consumption is significantly higher than with thiopental, regardless of the way in which it is expressed. Nevertheless, post-anaesthetic recovery occurs rapidly after discontinuation of the anaesthetic. It should be emphasized that these results were obtained in hospitalized, premedicated subjects. In a small number of out-patients who were given buthalitone sodium without premedication for minor procedures, we found the recovery even faster, in accordance with claims of European investigators.

It was our clinical impression that whereas in the thiopental series respiration of the subjects could be controlled almost routinely, this was next to impossible in the buthalitone sodium group. We take this as an indication of less respiratory depression and further experiments are in progress to objectivate this finding.

It may be argued that the data on recovery time show recovery from nitrous oxide anaesthesia rather than recovery from buthalitone sodium and that the interventions were carried out more under nitrous oxide than under buthalitone sodium anaesthesia. Even if this were conceded, the comparison with thiopental would still remain valid since identical techniques were used. The difference between the mean anaesthesia times of the two groups argues against such an assumption. This difference is "probably significant" in the statistical sense (Table

FIGURE 1. Variations in haematocrit, serum protein and protein fractions following buthalitone Na anaesthesia. The variations are expressed as percentage of the initial values, the vertical lines represent

I) and there is no reason to assume that the same surgeons took longer to perform an identical operation on comparable subjects in the one group than in the other. Since the period from the end of surgery to the reaction to stimuli is included in our definition of anaesthesia time, it may rather be this interval that is prolonged in the thiopental group in comparison with the buthalitone sodium series. While regrettably we lack for recovery from thiopental the detailed numerical data which were collected in the buthalitone sodium group, there is in our mind no doubt at all that such is indeed the case.

The series is much too small to form a definite opinion about the incidence of complications during the course of anaesthesia with buthalitone sodium. In the first few patients anaesthetized with this agent, hiccoughs and some transient

hypotension (lasting about 5 min.) were encountered. These side reactions were not seen again once we gained some experience with the drug, their appearance seems to be in direct relation with the speed of injection. Laryngospasm was notably absent.

The use of a 5 per cent solution is a departure from the manufacturer's recommendation of a 10 per cent concentration. The recommendation is based on the use of the agent in Europe where medico-legal considerations carry less weight than on this continent. After slight initial difficulties, we were completely satisfied with the 5 per cent concentration which has the added advantage that it handles very much like a 2½ per cent solution of thiopental.

Blood samples were drawn from the subclavian vein in order to avoid artefacts arising from the application of a tourniquet. In cases where a smaller vein was used, blood was withdrawn only after release of the tourniquet. The absolute concentration of each protein fraction was calculated from the total protein concentration and the percentage distribution of the electrophorogram. While the changes due to anaesthesia are small compared to variations from patient to patient, as can be seen in Table III, they are sufficiently uniform to establish a statistical significance when the per-anaesthetic changes themselves are studied (Table IV). Owing to the fact that the quantity of the different protein components present in the serum varies widely, these data cannot be used directly to determine whether or not the changes observed can all be reduced to one common factor or whether the behaviour of some fractions differs from the others. In order to make such a determination, the per-operative changes were expressed in percentages and a new set of σ'_M values was calculated to satisfy the original t values (Table IV). Using these data, it appears that variations among most of the fractions are due to chance and/or experimental error. The α_1 -globulin fraction however differs significantly in its behaviour from the other fractions (Table IV and Fig 1).

Postoperative changes in serum proteins are beginning to receive greater attention (16-21). Most investigations are initiated by surgeons and deal exclusively with changes occurring during the days following surgery. These changes—decrease in albumin, early increase in alpha-globulins and late increase in beta-globulins—are usually interpreted as manifestations of the adaptation syndrome. To the best of our knowledge, the present study offers the first evidence that similar changes can be detected as early as 20 minutes after the induction of anaesthesia, even when the surgical intervention is minimal. From all available evidence it would seem that they are the result of general response to stress rather than to any specific anaesthetic.

CONCLUSIONS

Buthalitone sodium has a shorter action than other thiobarbiturates now available. It appears to be free of harmful side effects and produces relatively little respiratory depression. These characteristics indicate that its field of greatest usefulness is anaesthesia for minor surgery and office and dental procedures, subject to the usual precautions with thiobarbiturates.

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