EPIDURAL AND NERVE BLOCK ANAESTHESIA WITH SYMPOCAINE¹

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NO KNOWN LOCAL ANAESTHETIC AGENT can be said to be ideal, but we have at hand a number of reliable agents which under average clinical conditions give adequate anaesthesia with a sufficient degree of safety. The pharmaceutical houses continue to present us with new substances in the hope that the nebulous ideal may be more nearly approached. A number of 2-alkoxy derivatives of procaine have been synthesized and investigated in animals. One of these is the 2-butoxy derivative first synthesized by Clinton and Salvador (1). Its structure is:

2-DIETHYLAMINOETHYL-4-AMINO-2-BUTOXYBENZOIC ACID

Luduen and Hoppe (2) studied the drug in animals with the following results. Compared with tetracaine, Sympocaine® (WIN3706) is 1.7 times more potent in producing threshold anaesthesia in the sciatic nerve of guinea pigs and 2.3 times more potent in producing threshold anaesthesia in rabbit corneas. It reaches its threshold irritant concentration (Trypan blue intradermal test) at one-third that of tetracaine. When it is injected intravenously the acute toxicity LD50 in mice (40 mg./kg.) is 2.3 times tetracaine, with values of 2.3 and 2.8 mg./kg. in rabbits and guinea pigs respectively. Subcutaneously, the LD50 in mice was about the same as tetracaine and one-fifteenth that of procaine.

From these data, it was assumed that Sympocaine was one and a half times as potent and as toxic as tetracaine. In man one could then use two-thirds the clinical dose of tetracaine as a guide, although the manufacturers suggested 15 mg. as the maximum dose. Moore (3) suggests a maximum dose of 80 cc. of 0.25 per cent tetracaine and Dodd (4) suggests 40-50 cc. of 0.1 per cent for nerve block but 200-300 cc. when used for infiltration. Hewer (5) quoting James (6) suggests 2 mg./lb. with a maximum of 300 mg. Using these standards 1.3 mg./lb. or 200 mg. of Sympocaine might be considered the maximum dose. We would like to suggest from our studies that 1 mg./lb. be considered an optimal dose.

<i>Authority</i>	<i>Maximum dose</i>	<i>Comment</i>
Moore	80 cc. of 0.25% or 200 mg.	
Dodd	50 cc. of 0.1% or 50 mg.	Nerve block
	300 cc. of 0.1% or 300 mg.	Infiltration
Hewer	2 mg./lb. body wt. or 300 mg	

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METHOD

In view of the suggested maximum dose of 15 mg., the initial concentration used was 0.1 per cent. This proved to be inadequate and so the concentration was increased until, by trial and error, the minimum effective concentration of 0.5 per cent was discovered. Sympocaine was then used without the addition of epinephrine, which would mask the characteristics of the drug. The patients were selected at random from the surgical lists and the appropriate block performed with the new agent.

RESULTS

In all 413 patients were anaesthetized. 175 for caudal blocks, 28 for caudal with trans-sacral (sacral) blocks, 41 for epidural blocks, 98 for brachial blocks, 47 for sciatic-femoral blocks, and 24 for miscellaneous blocks (superficial cervical, sciatic alone, intercostal, paravertebral).

The largest dose given to a patient was 400 mg. and the smallest was 30 mg. The age range was 15 to 88 years and the weight range was 98 to 350 pounds. The range of duration was one-half hour to five hours. The averages are shown in Table I.

TABLE I

Block	Body wt (lb)	Dose		Duration (hrs)
		Mg	Cc	
Caudal	164	111	22	2 0
Caudal and trans-sacral (sacral)	157	132	26	1 8
Epidural	157	97	19	1 9
Sciatic-femoral	161	172	34	2 1
Brachial	173	150	30	2 2
Miscellaneous	155	120	24	1 7

An earlier report on the use of Sympocaine in 100 caudal anaesthesias gave an average dose of 109 mg. and an average duration of 2 hours (7). Body weight was plotted against duration of anaesthesia for 30 brachial blocks using 150 mg. doses. No relationship could be defined. Dose was plotted against duration in 80 cases of caudal, sacral and epidural blocks in two age groups: 25-40 and 55-70. No relationship could be defined between dose and duration, nor could the age groups be separately defined. Age was plotted against duration at 100 mg. dose level for 32 males using caudal block. No relationship could be defined.

COMPLICATIONS

Failures

(a) In the *caudal* group there were eight (4.5 per cent) failures which could be attributed to difficulty with technique. One incomplete caudal was continued with as the operative lesion was on that side. None of the failures seemed due to poor drug action.

(b) In the *sacral* group one failure was due to spotty anaesthesia, while another was incomplete on one side.

(c) In the *epidural* group, one failure was probably due to poor technique and another was a partial failure. Two further failures occurred after an adequate dose of the drug and were suggestive of drug failure.

(d) There were two incomplete *brachial* blocks in which the cause for failure was uncertain.

(e) One *sciatic-femoral* block failed and this was almost certainly due to poor technique.

(f) In the miscellaneous group, one sciatic block failed due to poor technique.

Possible Evidence of Toxicity

(a) In the caudal group, there was one case each of: (i) generalized pilomotor response, (ii) generalized flush for one minute, (iii) drowsiness for ten minutes,

TABLE II
DETAILED LIST OF HYPOTENSIONS

Age	Sex	Weight	Operation	Dose (mg)	Onset	Duration (hrs)	Height	Comment
CAUDALS								
47	F	—	Haemorrhoid	100	10	2	T12	Apprehensive 130/80 106/70, V P ^a
62	M	135	T U R	45	4	—	T6	180/110-110/80, V P
31	M	145	Haemorrhoid	115	6	—	—	Very apprehensive 110/60-60/30
64	M	114	Rectal polyp removal	65	2	—	—	No unusual spread, patient prone and very flexed, V P
38	M	198	Haemorrhoid	125	1½	2	—	Faintness, hypotension, sweating, V P
64	M	190	T U R.	95	5½	3	—	No unusual spread 110/80-90/70 V P.
50	F	120	Haemorrhoid	70	1	3	—	Systolic fall 190-140 with nausea
EPIDURALS								
57	M	165	L I H	110	6	2½	T8-L2	Moderate fall, V P
61	M	160	L I H	75	4	1½	T8-S3	130/80-100/60
44	M	175	Vein stripping	100	8	—	—	Progressive hypotension, with progressive rise in level after injection
52	M	145	L I H.	65	6	1½	T8-S3	40 mins after onset sudden fall 96/54-64/34; no change in level or status of patient
57	F	—	Gastrostomy	125	5	1½	—	B.P fall, V P
75	M	172	R I H	75	12½	2	T8-L2	Hypesthesia 2-3 segments either way, 118/78-96/56 V P
68	M	140	R I H	85	7½	2	T3-?	130/60-90/50 V P
86	M		Strangulated I H	60	7½	1½	T10-L4	110/70-90/50 V P
33	M	161	Pilonidal cyst	100	3	2¼	—	Fall of 30 points systolic, V P
72	M	116	Gastrostomy	75	7	2¼	T4-?	120/80-95/60
SACRALS								
56	M	150	Proctoscopy polyp removal	250	15	2	T12 on L S3 on R.	B P. fall requiring V.P.

^aV P = Vasopressor given with satisfactory results

(iv) failure to respond to the spoken voice for a very short period, with spontaneous recovery.

(b) In the sacral and epidural groups there were no cases of toxicity.

(c) In the brachial block group four patients became drowsy and one felt chilly (doses in mg. 150, 225, 100, 300 and 125).

(d) One patient who received a sciatic-femoral block in which 250 mg. were used became apprehensive and "tremulous."

(e) There was no evidence of toxicity in the other groups.

Hypotension

Hypotension occurred in 18 cases among the epidural-type blocks: 10 epidurals (25 per cent); 7 caudals (40 per cent); and 1 sacral (3.7 per cent). Hypotension did not appear in the other groups of blocks. From Table II it can be seen that the cause of hypotension in these groups was more likely related to the form of block and consequent loss of sympathetic vasomotor control.

Evidence of Irritation

Transient stinging or burning on injection occurred in the groups of blocks other than the epidural type; these latter had skin wheals of procaine. In the brachial block group, 37 out of 98 patients had these: a high incidence of about 38 per cent. No evidence has appeared suggestive of any more serious form of irritation in the skin or deeper tissues. The preservative in the solution contains among other things 1:600 phenol and this will be modified if the drug is marketed.

DOSAGE

Caudals

This technique was used largely for rectal and perineal surgery. The chief dose groups were 50-75 mg. (39 cases); 76-100 mg. (65 cases) and 101-125 mg. (31 cases). The common doses were 15 cc. (75 mg.) or 20 cc. (100 mg.). On occasion, even these doses may give a higher level than desired, as can be seen from the examples in Table III

TABLE III
EXAMPLES OF EXCESSIVE SPREAD

Age	Sex	Weight (lb)	Dose (cc)	Level	Operation	Comments
47	F	—	20	T12	Haemorrhoid	B P fall
40	M	130	15	L1	Haemorrhoid	
31	F	—	23	T11	Haemorrhoid	
54	M	193	17	L1	Haemorrhoid	
27	M	168	20	T8	Ischio-rectal abscess	B P, fall
46	M	139	25	T3	Anal fistula	

Altogether, twenty-two (12.5 per cent) of the levels were too high; five (3 per cent) of these were excessively high, but only two could be related to generosity in dosage. It must be kept in mind that there is considerable variability in the anatomy of the region, in particular the volume, which can vary from 12 to 65 cc.

(8). Test doses of 5 cc. were used routinely and these were then followed by the main dose of a size thought to be adequate.

Epidurals

The spread in this form of block appeared to be good and an adequate 6 to 8 segment block can frequently be performed using only 15 cc. (75 mg.). Where a catheter is inserted into the space, this is suggested as the initial dose.

Brachials

The most common doses used were either 20 or 30 cc. (100 or 150 mg.). Both of these doses were effective and seemed to last about two hours; the smaller dose did not appear to be less reliable or less effective and is likely adequate for routine use.

Sciatic-Femorals

For the sciatic 20-30 cc. (100-150 mg.) were used commonly, for the femoral, 5-10 cc. (25-50 mg.) with satisfactory results.

DISCUSSION

Despite the evidence of toxicity in animals it seems fairly certain that, when used for the variety of blocks already mentioned, a dose of 1 mg./lb. is a safe dose of Sympocaine, and that this dose is not the maximal. The complications in the doses used appear to have been very few. The hypotensive episodes are almost certainly referable to the form of block (lumbar and caudal epidural), while evidence of systemic toxicity was chiefly seen as drowsiness in five patients (1.25 per cent). The only disturbing phenomenon was the high occurrence of irritation on intradermal injection, but this is very likely to be due to the phenol preservative contained in the solution.

The onset of anaesthesia with the agent is fast (4-5 minutes), and this is most in evidence in direct nerve blocks, for example, of the brachial plexus. However, with epidural blocks adequate conditions for surgery may not be present until fifteen minutes after injection. The duration is approximately two hours, with a variation between one and a half and two and a half hours.

Many more blocks than those discussed here have been performed. The group of cases mentioned are typical of the general impression which has been so good that Sympocaine is now our routine agent for nerve blocks.

SUMMARY

In all 413 patients were anaesthetized with Sympocaine 0.5 per cent without epinephrine. Most (175) of the blocks were cauda epidurals with a further 28 sacral and 41 thoraco-lumbar epidural anaesthetics. Possible toxic reactions were observed in 10 patients (2.5 per cent). Hypotension was noted in epidural type anaesthesia and was almost certainly related to the form of block. Temporary irritation occurred on intradermal injection in more than one-third of skin wheals, but this is considered to occur because the experimental solution contains 1:600

phenol. Onset is rapid, usually requiring 4-5 minutes, while duration of action varies between one and a half and two and a half hours. The most common doses for the several techniques are mentioned

Sympocaine 0.5 per cent used in doses between 15 and 30. cc has been found to be reliable, to have moderate spreading ability, adequate effect and little evidence of toxic reaction.

RÉSUMÉ

Nous avons pratiqué, chez 413 malades, une anesthésie avec de la sympocaine 0.5 pour cent sans épinephrine. La plupart des blocages (175) ont consisté en des épidurales caudales et, dans 28 cas, en des sacrées et, dans 41 cas, en des épidurales thoraco-lombaires. Chez dix malades (2.5 pour cent), nous avons observé des réactions qui ont été, il est possible, des réactions toxiques. Au cours des anesthésies épidurales, nous avons observé de l'hypotension qui était sans doute attribuable à la sorte d'anesthésie. Dans 33% pour cent des injections intradermiques, nous avons observé une irritation temporaire, mais à noter que la solution expérimentale contenait 1.600 de phenol. L'induction de l'anesthésie est rapide ne réquérant ordinairement que 4 ou 5 minutes et la durée varie de 1½ à 2½ heures. La Sympocaine 0.5 pour cent employé à des doses variant de 15 à 30 ml. s'est avérée constante d'action, possédant un certain pouvoir de diffusion, assez efficace et laissant de légères traces de réaction toxique.

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