TUBADIL IN OPHTHALMIC SURGERY* ITS EFFECT ON INTRA-OCULAR PRESSURE

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ON several occasions d-tubocurarine has been used intravenously in conjunction with local analgesia for ophthalmic surgery (Kirby, 1950; Farquharson, 1951). The object has been to administer just sufficient to provide a quiet, immobile field for the surgeon, without causing respiratory embarrassment or unpleasant subjective symptoms in the patient. Probably these requirements are never fulfilled entirely, the result being a compromise. It is debatable whether the conditions provided have any advantage over the standard local analgesic technique which incorporates a facial nerve block. Both methods have the disadvantage of a limited duration of effect, which, although adequate for any surgical procedure, will be insufficient to influence the post-operative period.

A technique which would provide ideal operating conditions and would also protect the patient from spasm of the orbicularis oculi during the ensuing 24-hour period, when the risks of such complications as iris prolapse are highest, would have obvious virtues. With this in mind, a preparation which liberated d-tubocurarine slowly from a wax base was investigated. The preparation chosen was Tubadil†, since the reports of its duration of effect in other fields of medicine were encouraging (Hoback, 1952; Fuller, 1950; Norcross, Robins, and Lockie, 1949).

Tubadil.—This preparation is a mixture of bees' wax, peanut oil, and oxy-cholesterols, containing 25 mg. d-tubocurarine per ml. When cold it is solid, but on gentle warming it becomes fluid. If given by deep intramuscular injection it is liberated slowly from this depot. There is experimental evidence which suggests that the toxicity of Tubadil (in terms of respiratory paralysis) is less than that of equivalent doses of intravenous d-tubocurarine in the ratios of 10:1 (intramuscular Tubadil) and 3.5:1 (intravenous Tubadil) (Gordon). These figures emphasize the slow liberation of the active alkaloid from the menstruum, and also demonstrate the safety factor of the mixture.

Injection Technique.—The ampoule of Tubadil is placed in water at about 60° C. (as hot as the hand can tolerate). When the contents have become fluid, the ampoule is shaken vigorously to ensure uniform mixing, and the chosen dose is then drawn up into a dry, sterile, syringe through a No. 1 hypodermic needle.‡

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† Registered trade name of Endo Products Inc. for a repository form of d-tubocurarine.

‡ A No. 1 hypodermic needle has an outer diameter of 0.81 mm. and a length of 38 mm., and is equivalent to a 21 S.W.G.

To avoid too rapid cooling of the mixture, which might make injection difficult, the syringe and needle should also be warmed.

The injection must be made into a muscle mass, preferably the gluteal, as a single insertion. Heat must not be applied nor the area massaged, since these measures may increase the rate of liberation of d-tubocurarine to a dangerous extent.

Previous Uses of Tubadil.—This drug has been used during the past 10 years for a variety of conditions in which muscle spasm has been present. Originally, indications were found in neurological diseases which included tetanus (Weed, Purvis, and Warnke, 1948; Honey, Dwyer, Smith, and Spalding, 1954). More recently it has proved of value in the relief of sphincter spasm and hence pain following anal operations (Malia, Lucas, Burns, and Whitacre, 1954). The doses have been adjusted to meet requirements, but with growing confidence in the safety of the preparation they have been increased to give better relaxation without causing undesirable side-effects.

Present Investigation

It was hoped that Tubadil would abolish the need for a facial nerve block by providing a relaxed orbicularis oculi at the time of operation, and preventing the tendency to "squeeze" during the early post-operative period. Tubadil was administered 2 hours pre-operatively to a group of patients about to undergo surgery for cataract extraction. Before receiving the drug, each individual was tested for vital capacity, hand grip with a dynamometer, and ocular tension.* 90 minutes later, before the injection of local analgesia and the beginning of surgery, these tests were repeated.

24 patients were chosen for the investigation, whose ages ranged from 42 to 85 years. Without selection they were divided into four groups of six subjects each. The first group received 0.75–1.25 ml. Tubadil, the second group 1.65–2.0 ml., the third group 2.5–3 ml., and the fourth group two injections of 1 ml. The injections were given 2 hours before operation, at the same time as premedication with intramuscular phenobarbitone.

Results

In none of these patients, even those who received as much as 75 mg. d-tubocurarine, was it possible to provide sufficiently relaxed eyelids to dispense with the necessity for a facial nerve block. Ptosis was seen on occasion, also a lateral nystagmus, suggesting partial paralysis of the external ocular muscles. Hand dynamometer readings showed little change, and although there was frequently a slight fall in vital capacity, this was insufficient to be considered of clinical significance. No subjective symptoms attributable to the Tubadil were observed either in these patients or in six others who received Tubadil in comparable doses for a further series of tests.

The most noticeable result of this investigation was the fall in ocular tension which was encountered in the majority of patients. The greatest

* Ocular tension was measured with a Schiötz tonometer (Weiss) and the same instrument was used throughout with a loading of 5.5 g. The results shown in the accompanying Tables are given all in mm. Hg.

falls occurred in those who had the highest ocular tensions initially, the maximal effect occurring approximately 2 hours after injection. In those patients who underwent surgery it was impossible to determine the duration of this fall in tension; in consequence, six patients who were being investigated medically for glaucoma were given Tubadil and the ocular tension was measured at 4-hourly intervals thereafter. It would appear that, in spite of varying the dose of Tubadil, the effect lasted for 15 to 24 hours in each patient, the duration bearing little relation to the amount injected (Table I). But it might be assumed from this evidence that the Tubadil would have exerted a considerable effect during the immediate post-operative period if these patients had been submitted to operation.

TABLE I
EFFECT OF TUBADIL IN SIX PATIENTS NOT UNDERGOING SURGERY

Age (yrs)	Sex	Initial Ocular Tension (mm. Hg)		Dose of Tubadil (ml.)	Lowest Ocular Tension (mm. Hg)		Fall in Ocular Tension (per cent.)	Duration of Effect (hrs)
		Right	Left		Right	Left		
82	F	45	42	3	25	27	44	20
52	M	40	35	3	10	12	25	23
44	M	35	50	2	25	25	50	17
33	F	60	33	2	30	25	50	23
66	M	22	22	1	12	15	45	16
73	F	30	30	1	20	21	33	15

Of the 24 patients who received Tubadil before surgery (Table II, opposite), eleven showed a fall in ocular tension. All of these remarked on their freedom from discomfort during the post-operative period. Slight or no changes in the ocular tension were found in six patients in whom the tension was almost within the range of normal at the outset. Once more, post-operative freedom from pain was noticeable. The remaining seven patients showed a rise in tension; in five this might be explained by the fact that the second reading was made by a different person—a factor which did not arise with the previous patients. One patient in this last group complained that the post-operative pain was more severe than after an extraction performed one year previously on the other eye.

In a small control group of six patients about to undergo cataract extraction without Tubadil, a similar series of tests (vital capacity, dynamometer reading, and ocular tension) was performed to assess the effect of any pre-medication that had been given. In this group, the ocular tension remained unchanged in four, showed a slight rise in one, and a slight fall in one (Table III, opposite).

Conclusions

It appears that Tubadil *per se* is capable of reducing the ocular tension for several hours. This implies that the mechanism must be due to factors

TABLE II
EFFECT OF TUBADIL ON 24 PATIENTS ABOUT TO UNDERGO CATARACT EXTRACTION

Group	Age (yrs)	Sex	Initial Findings				Dose of Tubadil (ml.)	Findings 90 min. after Tubadil Administration			
			Ocular Tension (mm. Hg)		Vital Capacity	Hand Dynamo- meter		Ocular Tension (mm. Hg)		Vital Capacity	Hand Dynamo- meter
			Right	Left				Right	Left		
(1) 0.75 to 1.25 ml.	73	M	18	10	1,100	15	1	14	24	1,000	15
	79	F	33	22	1,900	35	0.75	25	15	1,350	45
	65	F	27	33	1,800	35	1	22	33	1,700	33
	77	F	15	15	1,400	16	1	10	10	1,150	10
	73	M	42	42	2,100	20	1.1	25	25	1,650	18
	71	F	25	23	800	24	1.25	22	240	700	20
(2) 1.65 to 2 ml.	76	M	42	53	2,800	20	1.65	25	28	2,600	18
	54	M	18	18	2,700	47	1.7	30	30	2,300	42
	59	M	14	14	3,300	42	1.75	14	14	3,100	42
	67	F	22	22	1,600	32	1.8	17	17	1,550	28
	77	M	9	15	2,000	20	2	22	33	1,800	16
	67	M	14	7	2,450	14	2	10	10	2,100	14
(3) 2.5 to 3 ml.	59	F	22	18	1,600	27	2.5	22	27	1,300	21
	85	F	22	22	1,200	13	2.5	27	27	1,200	13
	84	F	18	18	1,550	15	2.5	27	22	1,600	14
	42	M	18	14	2,700	24	2.5	14	14	2,600	22
	72	F	22	22	1,400	34	3	18	18	1,200	27
	82	M	10	10	1,450	25	3	14	25	1,600	43
(4) 2 ml.	67	F	12	12	1,600	11	Two doses of 1 ml. each	12	10	900	11
	77	M	25	32	2,400	19		18	18	2,500	19
	68	F	22	27	1,300	15		18	18	1,500	15
	66	F	9	9	1,000	12		6	6	1,050	10
	54	M	18	18	3,650	22		14	10	3,650	19
	78	M	10	10	600	15		10	10	650	14

TABLE III
CONTROL SERIES OF SIX PATIENTS NOT GIVEN TUBADIL*

Age (yrs)	Sex	Ocular Tension				Effect on Ocular Tension
		Before Premedication		2 hours after Premedication		
		Right	Left	Right	Left	
79	M	22	22	22	22	Unchanged
78	M	14	25	14	25	Unchanged
64	M	18	18	27	22	Rise
78	F	9	11	13	9	Unchanged
63	F	15	22	12	15	Fall
74	M	9	15	12	15	Unchanged

* All patients received premedication with 2 gr. (120 mg.) phenobarbitone intramuscularly.

other than relaxation of the external ocular muscles, since it is recognized that the eye quickly accommodates itself to pressure effects from without. It is doubtful whether Tubadil serves any useful purpose in the routine preparation of the average patient who is to undergo cataract extraction, but in those with a high initial ocular tension, with its well-known attendant

risks, it should be possible to afford some protection for a limited period. We would therefore suggest that in patients in whom the risk of post-operative ocular complications of a similar nature might be expected, Tubadil deserves a more extended clinical trial.

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