CURARE IN OCULAR SURGERY*

REPORT OF 25 CASES

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CURARE, a drug extracted from two main plant sources of the natural orders *Manispermaceae* and *Strychnos*, was formerly obtained from S. American Indian tribes who used it as an arrow poison in hunting and warfare. The drug acted by paralysing the victim, a large enough dose being rapidly fatal. The important active principle ($C_{38}H_{44}O_6N_2$) is designated *d*-tubo-curarine.†

From the ophthalmologist's point of view, the special value of curare lies in its selective sequence of paralysis, affecting first the muscles innervated by cranial nerves, then the extremities, and lastly the trunk and respiratory muscles. Roche (1950) described the following sequence: transient blurring of vision, facial flaccidity, ptosis, paresis of the vertical ocular muscles followed by that of the horizontal group, relaxation of jaw, pharynx, larynx, cervical muscles, and horizontal rotators of the globe. The ocular muscles are the first to be affected and the last to recover.

The judicious use of curare enables the cataract surgeon to perform his task with greater delicacy and precision, since it renders the patient and his eyes quiet and relaxed. The rigidity and muscular spasm which may be caused by apprehension, fear, or worry, or may be reflex to pain and discomfort, are the source of many complications in cataract surgery, but although these disadvantages of local anaesthesia have long been recognized the risks attendant upon general anaesthesia are even greater. The search for an agent which would overcome muscular spasm and rigidity in general anaesthesia, and which would permit the lightening of such anaesthesia, has led to the application of the akinetic drugs of the curare group.

Curare has been employed in general surgery for the last 8 years, but its use in ophthalmology was reported first by Kirby (1949) and a little later by Clark (1949).

Earlier Investigations

Kirby (1949) used "Intocostarin" in over one hundred patients whose ages ranged from 24 to 48 years; 40 per cent. received 60 units, 20 per cent. 50 units, and 40 per cent. 40 units. In ten cases (10 per cent.) general akinesia did not develop, and palpebral, ocular, and general rigidity and spasm were retained to some degree, causing embarrassment during the operation, and in three of these ten cases vitreous was extruded.

Farquharson (1951) used curare in a series of 70 patients whose ages ranged

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† Three varieties of the crude preparation were formerly distinguished by the method of packing: (i) tube curare, shipped in bamboo tubes; (ii) calabash curare, shipped in dried gourds; (iii) pot curare, shipped in earthenware jars

from 37 to 87 years. The dose varied from 20 to 60 units (average 40). Five patients showed subjective symptoms for 5 to 7 minutes but these passed off before the section was made.

Cordes and Mullen (1951) used curare in 85 cases of the same age group, and were deeply impressed by the satisfactory relaxation obtained in difficult cases in which surgery without curare would have been complicated.

In summarizing their own observations and those of other workers, Cordes and Mullen state that the patient usually remains motionless after curarization has relaxed his arms and legs, and assumes regular respirations; his eye is motionless in the primary position and nystagmus is abolished. No traction or superior rectus suture was ever necessary. Even the anxious patients were sufficiently relaxed to drift off to sleep on the strength of their premedication. No deleterious effects were noted during surgery or in the post-operative period, except that in a few cases the surgeon felt that the eye was so soft as to retard the delivery of the lens.

Reduction in the loss of vitreous is the goal of most surgeons. Using curare, Clark (1949) noted no loss in 44 cases and Kirby had only three instances in one hundred cases; Cordes and Mullen, who had five cases in 85, claim that their subsequent cases have gone more smoothly though actual figures are not quoted.

Clinical Recommendations

Indications

- (1) "Bad actors", who are apprehensive and nervous in spite of good premedication.
- (2) "Squeezers", who, by closing the opposite eye forcibly, cause both eyes to roll upwards.
- (3) Patients who are deaf or who have language difficulty.
- (4) Patients with borderline senile dementia.
- (5) Patients with objective signs of being high surgical risks.

In all these clinical types the relaxation and control afforded by curare establish a safety margin not obtainable by other methods. Since it is impossible to anticipate the sudden complications which may arise during surgery, curare may well be used as a routine in every case of cataract extraction. Especially is this so in a country such as India, where the majority of patients are uneducated and also present language difficulties.

Contraindications

- (1) Myasthenia gravis: a sufferer from this disease is 20 times more sensitive than a normal man.
- (2) Marked renal insufficiency: this would unduly delay excretion of the drug.
- (3) Emphysema, asthma, or history of asthma.
- (4) Recent respiratory disease.

Administration.—Curare should be given by the intravenous route, as in this way it can be better controlled. The rate of administration should be regulated at 20 units per minute and the patient observed for the development of facial paralysis and ptosis. The total amount should depend on clinical judgment, rather than on any preconceived notion of age and weight, though a dose of $\frac{1}{2}$ unit per lb. body weight (average 50 units) is recommended by Roche (1950).

Nearly all the drug is disposed of by the body in 25 to 30 minutes, so that a patient can walk to his bed unassisted 30 minutes after a completely paralysing dose.

Present Investigations

An extensive survey of cataract operations performed at this hospital with regard to vitreous loss and the behaviour of the patient was undertaken by the present writers. Vitreous prolapse occurred in 10·2 per cent. of cases in 1948, 1949, and 1951, and in 13 per cent. in 1950. No important general effects were recorded.

Material.—A series of 25 cases was then operated upon after curare administration to assess its role in lessening the complication of vitreous loss. These patients were not selected except in so far as those in whom the drug was contraindicated (as above) were excluded.

Method.—Routine preparation of the patient was carried out and luminal used as premedicant (1 gr. at bed-time the night before, and 1 gr. one hour before the operation). Atropine gr. 1/100 was given 30 minutes before the operation to check excessive secretions from the upper respiratory passages. Topical anaesthesia was given by 2 per cent. anethane four times every 5 minutes.

Oxygen, adrenaline, eserine, prostigmin, a laryngoscope, and intubation requirements were kept ready for emergencies, but none was needed.

The patient's weight, blood pressure, respiration, blinking reflex, and ocular tension were recorded just before the injection (Table I, overleaf). This was usually given through a small needle into a vein in the cubital fossa; it may be given into the back of the arm, but not into the leg because the anaesthetist must be as near to the chest and head as possible to keep a close watch on the respiration.

Dose.—No attempt was made to administer curare by any preconceived dosage schedule, the anaesthetist being guided by the clinical appearance of the patient. The drug was given sufficiently long before the eye was to be sectioned, for any untoward reactions to be over before the surgical operation was begun. Curare usually requires 3 to 5 minutes to reach its peak of action which then lasts for at least 20 to 25 minutes. The total dose should not produce any but the most minimal untoward and subjective reactions, and its maximum effect must be present when the eye is opened and the cataract is being extracted.

Initially, 4 mg. (*i.e.*, 28 units) of *d*-tubo-curarine chloride (Abbotts) were given in one minute and the patient was observed for the development of ptosis. If this did not develop within 2 to 3 minutes, another 1 to 2 mg. were given in one minute, and the dose was repeated after 3 minutes if necessary—a close watch being kept upon the respiration and facial paresis. The aim of the dose is to ensure that the patient loses his power to squeeze, the eyeball remaining stationary, and the patient quiet and relaxed. In no case was it necessary to give a supplementary dose once the operation was begun, as in every instance the procedure was all over before the patient recovered the power to squeeze. Blood pressure, respiration, and pulse were taken first after the operation and 30 minutes later (Table I, overleaf).

TABLE I

Case No.	Age (yrs)	Weight (lb.)	Total Dose (units)	Intra-Ocular Pressure* (mm. Hg)	Blinking Reflex* (No. per min.)	Blood Pressure+	Pulse+	Respiration+
1	60	116	42	25 20	18 2	130/64 130/64	80 82	20 24
						128/62 130/64	80 81	26 22
2	40	130	49	22 18	15 2	140/90 140/90	72 74	30 34
						140/90 142/94	84 74	34 32
3	52	94	56	28 22	16 5	150/80 140/90	72 84	20 20
						145/94 145/90	80 80	18 20
4	54	96	56	25 20	20 2	135/80 110/80	100 100	24 24
						110/80 110/80	110 100	24 25
5	47	124	63	22 15	18 3	160/100 160/100	84 100	24 25
						160/100 160/100	100 100	25 24
6	50	94	68	28 22	18 3	120/80 110/80	80 72	20 16
						110/80 110/80	80 80	16 16
7	66	96	64	25 20	20 3	120/90 120/90	84 100	16 20
						120/90 120/90	100 100	15 15
8	50	122	48	22 20	20 1	130/80 130/76	88 84	24 20
						130/76 130/70	80 80	20 20
9	50	78	42	25 18	18 1	122/80 122/80	72 80	25 20
						122/80 122/80	80 80	20 20
10	60	108	56	22 18	10 2	135/80 140/80	72 72	16 16
						140/80 140/80	72 72	16 16
11	55	88	49	25 18	10 1	150/70 150/90	72 70	20 25
						150/90 150/90	72 72	20 20
12	45	108	56	25 18	12 3	120/70 120/60	72 72	20 16
						120/70 120/70	70 70	18 18
13	50	101	56	22 18	20 2	120/80 120/80	84 88	16 16
						120/80 120/80	80 80	16 16
14	40	100	40	25 20	16 5	140/110 140/110	70 70	20 20
						138/110 140/110	70 72	20 22

(continued)

TABLE I—*continued*

Case No.	Age (yrs)	Weight (lb.)	Total Dose (units)	Intra-Ocular Pressure* (mm. Hg)	Blinking Reflex* (No. per min.)	Blood Pressure ⁺	Pulse ⁺	Respiration ⁺
15	50	88	42	22 18	18 2	140/110 138/108	68 68	18 20
						140/110 140/110	68 68	25 28
16	50	102	49	22 15	16 3	140/84 140/84	72 72	19 19
						140/84 140/84	72 72	19 19
17	50	108	42	25 18	16 6	120/60 120/60	73 72	19 19
						120/60 120/60	72 73	19 19
18	40	80	35	25 20	18 3	150/90 150/90	62 62	17 17
						150/90 150/90	62 62	18 17
19	50	100	42	20 15	20 6	130/40 128/40	68 68	18 20
						128/40 128/40	68 68	25 17
20	50	102	35	25 20	16 2	90/50 90/50	62 60	18 18
						90/50 90/50	60 60	20 20
21	50	98	35	25 18	18 4	130/90 130/90	72 72	20 16
						128/90 128/90	70 70	18 20
22	45	100	42	22 18	20 3	130/90 130/90	82 80	18 18
						130/90 130/90	80 80	18 18
23	68	120	49	25 18	18 6	130/90 128/85	70 72	19 18
						128/85 128/85	72 72	18 18
24	59	125	49	25 20	16 6	150/90 150/90	80 82	20 18
						150/90 150/90	80 80	18 18
25	60	100	42	20 15	20 2	140/80 135/80	73 73	20 18
						135/80 135/80	73 72	18 20

* Intra-ocular pressure and blinking reflex were tested before and after the injection.

⁺ Blood pressure, pulse, and respiration were recorded just before and just after the injection, and just after and then half an hour after the operation.

Discussion

Kirby (1949), to whom the idea of using curare in cataract surgery is largely due, lists five desiderata in the proper conduct of cataract surgery:

- (a) sedation,
- (b) analgesia,
- (c) anaesthesia,
- (d) palpebral and global akinesia,
- (e) basal or general akinesia.

The first three and to some extent the fourth are easily controlled in any operating theatre; but nevertheless vitreous prolapse may occur in a certain percentage of cataract extractions, especially if the patient is nervous and uncooperative. In India, where many patients are illiterate or speak a language different from that of the surgeon, it is more than ever important to find a means of securing complete relaxation and immobility.

Dosage.—Our patients' ages ranged from 40 to 66 years and the dose from 42 to 68 units (average 54). Our experience is based on *d*-tubo-curarine chloride (10 mg./ml.); the initial dose required to produce ptosis ranged from 28 to 36 units, which is slightly lower than that suggested by Roche (1950), who reports an average dose of 38 units (Table II). Roche recommends a dose of $\frac{1}{2}$ unit per lb. body weight as a rough guide to the total dose, but other workers deprecate any preconceived dosage according to weight or age, as the results are unpredictable. Drucker and others (1950) pointed out that the effects of curare vary in different individuals, and we ourselves could find no relationship between weight or age and the dose required.

Roche reports that patients premedicated with barbiturates require a higher dose of curare than those who are not. Cordes and Mullen point out that Roche's observations do not conform with the generally-accepted view; in our series the dose required was higher where premedication was not very satisfactory than in cases where it was satisfactory.

TABLE II
DOSAGE

Author and Date	Average Dose (units)		Total Cases
	For Ptosis	For Ocular Surgery	
Roche (1950) 	38	50	50
Kirby (1949) 	Not quoted	40 cases—63 20 cases—50 40 cases—40	100
Farquharson (1951) ...	Not quoted	44	70
Cordes and Mullen (1951)	Not quoted	Not quoted	70
Present Series (1952) ...	28 to 35	54	25

Duration.—Our results conform with those of other workers in that the average duration of action of the drug was 26 to 30 minutes.

General Effects.—Like Drucker and others (1950), we found no remarkable effect on the autonomic or central nervous system. The subjects showed no signs of cerebral depression. Changes in the blood pressure and pulse rate were negligible, and though in a few cases we noted that the rate of respiration was increased, it usually remained unchanged. Roche's observations are similar, while Drucker and others (1950), though making no

mention of the respiratory rate, think that there is a reduction in vital capacity. At most the changes in respiration and vital capacity are inconsistent and inconclusive.

Local Effects.—No ocular prominence was noted in our cases, nor was there any evidence of Horner's syndrome. The pupil, as reported by Drucker and others (1950), showed no significant alteration. In our series as in those of other workers the blinking reflex was considerably reduced (Table III).

TABLE III
LOCAL EFFECTS

Author and Date	Blinking Reflex	Intra-Ocular Pressure		No. with Vitreous Prolapse	Total Cases
		Amount of Fall	No. of Cases Showing Fall		
Roche (1950) ...	Reduced to 8 or less per min.	2 to 4 mm. Hg without premedication	15	Not quoted	50
		4 mm. Hg with Nembutal premedication	18		
Kirby (1949) ...	Not quoted	Average 3 mm. Hg	29	3	100
Clark (1949) ...	Not quoted	Not quoted		Nil	44
Farquharson (1951)	Not quoted	Not quoted		Not quoted	70
Cordes and Mullen (1951)	Not quoted	Not quoted		5	85
Present Series (1952)	Average reduced to 4 per min.	2 to 7 mm. Hg (average 6 mm.)	25	Nil	25

Duke-Elder (1938) has shown that in animals the pressure in the eye falls by almost half when paralysis of the voluntary muscles is produced by curare though there is no fall in the systemic blood pressure. Roche (1950), Duke-Elder (1938), and Gifford (1946) have demonstrated a measurable though slighter fall in intra-ocular pressure after curarization in human beings, Drucker and others (1950) state that there is no significant change in intra-ocular pressure after curarization, regarding such changes as they themselves noted as experimental errors.

In our series the intra-ocular pressure fell by 2 to 7 mm. Hg in every case, and we think that, though this drop is small, it may be of value in operating upon glaucomatous eyes. Further work on this point will be presented subsequently. In no case did we find the eyeball so soft as to present difficulty in extraction of the lens.

Finally, no doubt largely because of the co-operative state of the patients

and the slight lowering of the ocular tension induced by curare, no case of vitreous prolapse occurred in this series.

Summary

(1) The akinetic properties of curare offer a means of keeping cataract extraction patients quiet and relaxed during operation.

(2) The technique of premedication and administration is described and indications and contraindications listed.

(3) The results in 25 cases who received *d*-tubo-curarine chloride as an aid to local anaesthesia for global akinesia in cataract surgery are compared with others reported in the literature.

(4) It is concluded that small doses of curare with proper premedication enable the surgeon to carry out a cataract extraction with precision and ease by eliminating squeezing, ocular mobility, and nervousness. It is affirmed that curare is a valuable adjuvant in cataract surgery.

The work was done under the guidance of Prof. R. S. Varma with the permission of the Principal, H. N. Bhatt. We are very grateful to Dr. M. N. Nagu for his close co-operation and interest in the administration of the drug.

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NOTE

A letter has recently been received from Dr. A. M. Girgis of the Coptic Hospital, Cairo, Egypt, in which he states that 2 years ago he started to use Mephenesin in the form of Myanesin Elixir in intra-ocular operations. He would be interested in the comments of other surgeons who have used this preparation.