4-Hydroxybutyrate narcosis for ophthalmic surgery

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4-Hydroxybutyrate (Gamma-OH, Egic) was introduced into anaesthetic practice by Laborit, Buchard, Laborit, Kind, and Weber (1960) in France. It has been used extensively in America and Europe as a hypnotic. Its use in anaesthesia in Great Britain was discussed at a symposium at the Royal Society of Medicine (Gamma Hydroxybutyric Acid, 1968), and further information in the British literature is provided by Robertson (1967) and Tunstall (1968a). It seemed to us that 4-hydroxybutyrate could be used to produce a light level of unconsciousness for patients undergoing ocular surgery with local anaesthesia. Preliminary studies were carried out on patients undergoing extraocular operations to assess its suitability for intraocular procedures. The technique was found to be satisfactory and this paper describes its use to maintain unconsciousness in a series of patients undergoing ophthalmic surgery. The results are compared with those from another series who were given a conventional general anaesthetic similar to that described by Kaufman (1967). The changes in intraocular pressure are described elsewhere (Wyllie, Beveridge, and Smith, 1972).

Pharmacology

4-Hydroxybutyrate is the sodium salt of gamma-hydroxybutyric acid. It is a basal hypnotic which acts on the cerebral cortex directly with no subcortical action, and therefore has no analgesic properties. An analgesic supplement, however, depresses reflex activity and allows the dose of 4-hydroxybutyrate to be reduced from 70 to 40 mg./kg., as recommended by Tunstall (1968b). There is bradycardia and a slight fall in cardiac output which can be reversed by atropine (Virtue, Lund, Beckwith, and Vogel, 1966). Surgical stimuli may cause hypertension, tachycardia, and a rise in cardiac output. These reactions can be prevented by a phenothiazine, *e.g.* perphenazine, which depresses the reticular activating system (Vickers, 1968). A short-acting barbiturate, *e.g.* methohexitone, hastens induction and also eliminates the clonic movements which are an occasional accompaniment of 4-hydroxybutyrate narcosis.

Methods

339 patients were studied in this series, of which 64 per cent. were women. 168 patients received 4-hydroxybutyrate and 171 had conventional general anaesthesia. The groups were comparable for age and sex. The ages ranged from 27 to 92 years (mean 68 : S.D. 11.5). All patients were assessed preoperatively as fit for anaesthesia. 27 patients had diabetes mellitus and three suffered from myotonic dystrophy. There was the usual high incidence of cardiovascular and respiratory disease associated with elderly ophthalmic patients.

The patients were undergoing elective ocular operations as shown in the Table.

Table *Number of operations and anaesthetics used*

<i>Surgery</i>	<i>4-hydroxybutyrate</i>	<i>General anaesthesia</i>
Cataract extraction	134	131
Filtration operation for glaucoma	22	27
Correction of strabismus	6	4
Other	6	9
Total	168	171

STANDARDIZATION

The techniques were standardized as far as possible. All patients received nitrazepam 5–10 mg. on the previous night. Intramuscular premedication 1 hour preoperatively consisted of an analgesic, methadone 5–10 mg., an antiemetic, perphenazine 2·5–5 mg., and atropine 0·3–0·6 mg. Methohexitone was the induction agent. 4 ml. 4 per cent. prilocaine were applied topically to the mouth and pharynx in all cases.

DIFFERENCES BETWEEN GROUPS

The essential differences between the two groups were as follows:

4-hydroxybutyrate group

Unconsciousness was maintained with 4-hydroxybutyrate. Reflexes were obtunded by local anaesthesia to the eye. These patients did not receive suxamethonium and the trachea was not intubated.

General anaesthesia group

These patients received suxamethonium and were intubated. Unconsciousness was maintained and reflexes obtunded by nitrous oxide, oxygen, and halothane. They were extubated under deep halothane anaesthesia to avoid laryngeal spasm and coughing.

DETAILS OF 4-HYDROXYBUTYRATE TECHNIQUE

Induction

Through an indwelling intravenous needle 4-hydroxybutyrate is injected in a dosage of 40–50 mg./kg., followed by methohexitone 1 mg./kg. The mouth and pharynx are sprayed with 4 ml. 4 per cent. prilocaine and a Guedel airway is inserted. Oxygen at 3 litres/min. is given *via* a catheter inserted into the Guedel airway to prevent hypoxia which might result from the close approximation of sterile drapes to the patient's face.

Maintenance of the airway

Patients who have been rendered unconscious with 4-hydroxybutyrate maintain a clear airway without assistance when the head is turned to the side. This is not possible in ophthalmic surgery, so it is necessary to support the jaw either manually or mechanically. A device for this has been made from a Guy's suspension apparatus for the Boyle-Davis gag as shown in Fig. 1. The supporting rod was out to 10 cm. and a cork fixed to the end. The breast plate and cork are cushioned with foam rubber and the chain with rubber tubing. The device is shown in use in Figs 2 and 3 with the ratchet adjusted to the required position. A piece of strapping is applied over the chin and cork as shown, to prevent accidental displacement.

FIG. 1 *Apparatus* FIG. 2 *Gag in place, side view* FIG. 3 *Gag in place, general view****Local anaesthesia***

To render the operative field analgesic, 3 per cent. cocaine eye drops are instilled into the conjunctival sac, including both fornices, 20 min. before operation. Bupivacaine 0.5 per cent. with adrenaline 1 : 200,000 is injected at the following sites:

- (a) Lid suture area (0.5 ml.)
- (b) Retrobulbarly (1.5 ml.)
- (c) O'Brien's site for facial block (5 ml.) (Stallard, 1965).

This local anaesthetic agent is used because its longer action delays movement of the orbicularis oculi. To give the retrobulbar injection the globe is rotated upwards and adducted using fixation forceps.

Maintenance of unconsciousness

From experience of the narcotic in another field (in cardiac catheterization and angiography in children), it has been found that the duration of unconsciousness in the dosage used cannot be guaranteed over 45 minutes, so in cases in which the operation is to take longer than usual an increment of 4-hydroxybutyrate of 10 mg./kg. body weight is given 45 min. after induction. Likewise, to prevent reflex movement during peak stimuli, increments of methohexitone 10–20 mg. are given. We have found that such peak stimuli occur during injection of the local anaesthetic agent, insertion of the superior rectus suture, and removal of the lens. After operation the patient is turned on his side and transferred to the recovery room. The Guedel airway is left in position.

Results

OPERATIVE PERIOD

General state

In spite of some degree of hypotension (see below), the patients were well perfused and there was no evidence of cyanosis or sweating. Respiration was maintained at the pre-induction rate and depth in the majority of cases. In a few patients, periodic breathing was observed, but this is a well-known feature of 4-hydroxybutyrate narcosis and is unimportant in clinical practice.

Operating conditions

Good operating conditions are obtained with 4-hydroxybutyrate. The eye is soft and, as shown in Fig. 4, not congested.

FIG. 4 *Uncongested eye after use of 4-hydroxybutyrate*

Fig. 5 (opposite) shows the congested eye frequently associated with general anaesthesia. The fall in intraocular pressure with 4-hydroxybutyrate is described elsewhere (Wyllie and others, 1972).

FIG. 5 Congested eye associated with general anaesthesia

Complications

Operation was postponed in four cases. In one patient in each series this was because of hypotension following premedication. Another patient in the general anaesthesia group developed cardiac failure on induction and in the 4-hydroxybutyrate group there was one case of retrobulbar haemorrhage. This occurred in one of the early cases before the technique of globe rotation was adopted. Two patients having 4-hydroxybutyrate and one having general anaesthesia sustained loss of vitreous. Two cases in each series coughed during the operation, and there was one case of severe laryngeal spasm on extubation in the general anaesthesia group.

Arterial hypotension occurred throughout the series, but was significantly greater in those having general anaesthesia. The maximum fall in systolic blood pressure during operation was calculated and expressed as a percentage of the corresponding preinduction value. In the 4-hydroxybutyrate group the range was 0 to 67 per cent. (mean 19 per cent.; S.D. = 12). In the general anaesthesia group the corresponding range was 0 to 64 per cent. (mean 29 per cent.; S.D. = 17). There is a significant difference between these values ($t = 5.1$; $P = 0.01$). Although the maximum fall in blood pressure was occasionally large, it is worth noting that we have taken the lowest recorded reading for purposes of the calculation, and in most instances this was an isolated one. In the 4-hydroxybutyrate group three patients were given methoxamine to restore satisfactory levels of blood pressure; of the others nine required methoxamine.

POSTOPERATIVE PERIOD

Immediate results

Postoperative hypotension was compared in the same manner and was also greater in those having general anaesthesia. In the 4-hydroxybutyrate group the values obtained ranged from 0 to 67 per cent. again (mean 21 per cent.; S.D. = 11). In the general anaesthesia group the range was 0 to 71 per cent. (mean 29 per cent.; S.D. = 15). This difference is again statistically significant ($t = 4.9$; $P = 0.01$).

The recovery time was taken as the time from transfer of the patient from the operating theatre until full return of consciousness. This was longer and more variable in the 4-hydroxybutyrate series, ranging from 0 to 130 min. (mean 58 min.; S.D. = 39). In the general anaesthesia group the range was 5 to 65 min. (mean 18 min.; S.D. = 11). This difference is highly significant ($t = 11$; $P = 0.001$). Characteristically, patients awoke from 4-hydroxybutyrate suddenly but quietly and were immediately orientated. Only three

were confused on awakening compared with thirteen in the general anaesthesia group. In the 4-hydroxybutyrate group three patients awoke as the dressings were applied. Coughing on rejection of the Guedel airway occurred in 8 per cent. of cases in the 4-hydroxybutyrate series compared with 20 per cent. of cases in the others. Coughing was closely associated with a history of smoking and bronchitis.

Later complications

Vomiting occurred in 5 per cent. of the 4-hydroxybutyrate group and in 14 per cent. of the general anaesthesia group. In the latter, this was classed as severe and intractable in three cases. An additional 4 per cent. of patients in both series complained of nausea only. Confusion developed a few days after operation in 3 per cent. of the 4-hydroxybutyrate group and in 6 per cent. of the others. One patient who had had general anaesthesia required transfer to a psychiatric hospital for treatment of paranoia.

There was a minor transient pyrexia (99–100°F.) in 18 per cent. of cases in both series. Chest infections requiring antibiotic therapy occurred in 2 per cent. of patients in the 4-hydroxybutyrate group and in 5 per cent. of patients in the general anaesthesia group. There was a 2 per cent. incidence of urinary retention in all patients and one case of deep vein thrombosis in each group. 6 per cent. of cases in both series had developed hyphaema before the first dressing and two cases of iris prolapse associated with vomiting occurred in the general anaesthesia series. One of the disadvantages of 4-hydroxybutyrate was the 9 per cent. incidence of superficial phlebitis at the injection site. In 2 per cent. this was severe. In the general anaesthesia group 4 per cent. of patients admitted to “suxamethonium pains”—none complained spontaneously. Endotracheal intubation was associated with the usual high incidence of sore throats (16 per cent.) None of the 4-hydroxybutyrate group complained of this.

PATIENT PREFERENCE

In the whole series, all patients but one who had not had previous ophthalmic surgery preferred to be “asleep” for their operation. Surprisingly, however, in those who had previously had local anaesthesia with sedation one half would have preferred local anaesthesia again—a tribute to the efficacy of local anaesthesia in ophthalmic surgery. On the other hand, several patients who had previously experienced general anaesthesia consisting basically of a mixture of nitrous oxide, oxygen, and halothane have spontaneously commented on the absence of “hangover” after 4-hydroxybutyrate and the presence instead of a feeling of wellbeing.

Discussion

An attractive feature of this technique is the soft white eye which is achieved. The photographs illustrate the difference in appearance between the eyes of a patient having 4-hydroxybutyrate and those in a patient breathing a mixture of nitrous oxide, oxygen and halothane through an endotracheal tube. Since intubation is not part of our technique, there is no assault on the trachea and therefore no stimulus to coughing either on extubation or in the postoperative period. Except where the patient was a heavy smoker, coughing has not been a problem. On the other hand, where there is a risk of regurgitation, as in hiatus hernia or emergency surgery, this technique should not be employed since endotracheal intubation is then mandatory.

An advantageous feature of recovery from 4-hydroxybutyrate is the absence of confusion.

Patients may be unconscious and unrousable one moment and fully conscious and orientated the next. Although it cannot be hurried, awakening is sudden but calm. 4-Hydroxybutyrate is known to cause sickness: the fact that this has not been a prominent feature in our series is attributed to the phenothiazine included in the premedication. In addition, postoperative medication with an antiemetic is always prescribed, so that if a patient complains of nausea prophylaxis can be applied forthwith.

In the early stages of the series, several elderly male patients were incontinent of urine after going back to the ward. This was probably due to the relaxation of sphincter tone which may accompany unconsciousness with 4-hydroxybutyrate. The nursing staff are now careful to ensure that all patients come to theatre with an empty bladder, and there has been no further trouble from this source. Steel (1968) found that 4-hydroxybutyrate produced occasional psychological purgings of a sexual nature and released a cancerophobia in some patients. We did not expect, and did not find, any evidence of this in our elderly ophthalmic patients. One of the difficulties associated with standard general anaesthesia in this age group is the hypotension which may occur whether the patient is breathing spontaneously or is artificially ventilated. With 4-hydroxybutyrate there was indeed a fall in blood pressure in most of our patients, but in only three was it deemed necessary to give a vasopressor drug. Usually the fall in blood pressure was comparable to that expected in normal sleep. This may be one of the factors contributing to the low incidence of postoperative confusion.

The main disadvantage of the technique is undoubtedly the unpredictable duration of unconsciousness. Although there have been no particular problems attributable to this, it does necessitate a nurse staying with the patient until consciousness returns, and although she may not have to support the jaw (the Guedel airway being left in position) she cannot perform other ward duties. On the other hand, she can look after several patients at the same time.

Summary

4-Hydroxybutyrate is an ideal agent to produce basal narcosis for surgery under local anaesthesia. In ophthalmic surgery a soft white eye is obtained, and there is a low incidence of operative and postoperative complications.

We wish to thank Mr. C. Cockburn, Mr. M. G. Lyall, and the Staff of the Eye Department, Woodend General Hospital, Aberdeen, for allowing us to study patients under their care, and Dr. M. E. Tunstall for his encouragement during the development of the technique. We also thank Egic and Servier Laboratories for supplies of 4-hydroxybutyrate.

References

- KAUFMAN, L. (1967) *Proc. roy. Soc. Med.*, **60**, 1275
 LABORIT, H., BUCHARD, F., LABORIT, G., KIND, A., and WEBER, B. (1960) *Agressologie.*, **1**, 549
 ROBERTSON, J. D. (1967) In "Recent Advances in Anaesthesia and Analgesia", ed. C. L. Hewer, 10th ed., p. 655. Churchill, London
 STALLARD, H. B. (1965) "Eye Surgery", 4th ed., p. 75. Wright, Bristol
 STEEL, G. C. (1968) *Proc. roy. Soc. Med.*, **61**, 825
 GAMMA HYDROXYBUTYRIC ACID SYMPOSIUM (1968) *Ibid.*, **61**, 821
 TUNSTALL, M. E. (1968a) *Brit. med. J.*, **1**, 315
 ——— (1968b) *Proc. roy. Soc. Med.*, **61**, 827
 VICKERS, M. D. (1968) *Ibid.*, **61**, 821
 VIRTUE, R. W., LUND, L. O., BECKWITT, H. J., and VOGEL, J. H. K. (1966) *Canad. Anaesth. Soc. J.*, **13**, 119
 WYLLIE, A. M., BEVERIDGE, M. E., and SMITH, I. (1972) *Brit. J. Ophthalm.*, **56**, 436