CLINICAL EVALUATION OF SYNCURINE® (DECAMETHONIUM BROMIDE)—A TWO YEAR STUDY *†‡

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Since we first reported our experience with decamethonium bromide (syncurine®) two years ago (1), we believe that we have gained enough knowledge concerning this drug to make a few definite conclusions and recommendations. Some of these conclusions are slightly at variance with those contained in our preliminary report.

Syncurine has been used at the George Washington University Hospital in 2,403 cases. During the same period of time, 21,139 anesthesias of all kinds were employed, including local, spinal and general anesthetics. In approximately one-half of the cases in which it was used, the drug was employed primarily to provide relaxation for endotracheal intubation. It has been used twenty-six times for laryngoscopy or bronchoscopy in conjunction with pentothal® anesthesia. In obstetrics it has been used in 27 cesarean sections and 33 vaginal deliveries. The remainder of the cases represented operations in all fields of general and specialized surgery.

Methods

The patients who received syncurine during operation represented all age groups and all classifications of physical status. The anesthetists were, for the most part, residents in anesthesiology under the supervision of qualified anesthesiologists.

In general surgery the common method of administration was to induce relaxation by slow intravenous injection of 1 to 2 mg. of syncurine following the skin incision. Supplementary doses were given at intervals as needed. An attempt was made to keep the total dose between 4 and 6 mg., but this amount was exceeded occasionally. Variations in this technique were used for endotracheal intubation and in obstetric cases.

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For intubation, syncurine was given usually in a 2 mg. dose following induction of anesthesia with pentothal. Cocaine, 5 per cent, was almost routinely employed in a topical spray to the larynx. Oxygen or gas-oxygen was frequently given in the three to five minute interval between injection of syncurine and the beginning of laryngoscopy. In preparing for bronchoscopy a similar routine was followed.

In the few obstetric cases, the administration varied with the type of procedure. For cesarean section, syncurine was given to prepared and draped patients concurrently with induction with pentothal. Anesthesia was maintained with pentothal-ethylene-oxygen. During vaginal deliveries, syncurine was given to patients under ethylene-oxygen anesthesia at about the time forceps were applied to the fetus. The obstetrician then gradually exerted traction with the forceps against the relaxing perineum. An average of 2 mg. was used with obstetric patients.

Anesthetic agents employed in the series included pentothal, surital®, nembutal, nitrous oxide, ethylene, ether, avertin, and cyclopropane. The latter two were used least. In nearly all cases, the syncurine was administered separately from the intravenous barbiturate.

RESULTS AND DISCUSSION

In the evaluation of effects of a drug in clinical anesthesia, so many uncontrollable variables are present that statistical estimation of the drug's worth is difficult. Among the variables, which affect the quality of relaxation, are the demands of the individual surgeon, site of operation, size of incision, skill of the anesthetist, anesthetic drugs used, types of retractors employed and the individual requirements of the patient. This last item, in the evaluation of syncurine, may be the most variable factor of all.

After considerable experience with syncurine, we found that its properties adapted it well to certain procedures but rendered it less suitable for others. Among its properties are rapidity of action (two to three minute onset) and relatively short duration of action (twenty to thirty minutes). Another property, of which we became more cognizant as time went along, was that of tachyphylaxis. This latter characteristic, which applied certainly to the curarizing property of syncurine, causes repeated doses to be less effective than the original dose in producing satisfactory relaxation, at least in some individuals. As has been suggested by other investigators, syncurine appears to antagonize itself when repeated doses are given (2, 3). Still another property, which is a more favorable one, is that the drug has exhibited no histamine-like activity; we have seen no blood pressure falls or bronchospasms attributable to this drug (4). Absence of bronchospasm probably makes syncurine safer than other drugs in the asthmatic patient.

A characteristic of syncurine which may be a troublesome one to the anesthetist is its variability of action from patient to patient. The drug appears to be less potent in those patients who have a high tolerance to other hydrocarbons (for example, pentothal) used in anesthesia, for instance, in the alcoholic patient or the one who is habituated to barbiturates, paraldehyde, or other hypnotics. Occasionally, however, tolerance to the curarizing effects of syncurine is seen in patients who require only normal amounts of other agents to maintain adequate depth of anesthesia.

Lastly in the summary of the properties of syncurine, we have found that it is not particularly "sparing of respirations" as was first thought (5, 6). This has never constituted a hazard in our experience, because the anesthetists have been quick to employ manual respiratory support. The instances of apnea and hypopnea which have occurred have been of short duration (rarely over ten minutes) and have been characterized by rapid return of normal tidal exchange once the peak effect of the drug has passed.

We have never thought that endotracheal intubation is required in every patient who receives syncurine, as recommended by Foldes (7), but we routinely use oropharyngeal airways and keep endotracheal equipment on hand for use when indicated. Of course, oxygen equipment is always on hand, and it is frequently used prophylactically.

With these properties of syncurine in mind, we would like to discuss its use in various types of procedures. Among the abdominal operations in which syncurine was used, the most satisfactory results were obtained in lower abdominal surgery, particularly in those operations which required less than one to one and a half hours. An initial dose of 2 mg. usually sufficed to provide adequate exposure on opening the peritoneum. Placing of packs, use of Trendelenburg position and, in gynecologic procedures, the use of Balfour type retractors aided the anesthetist in maintaining a good operative field. Frequently, additional syncurine was not needed until just before closure was begun. Usually not more than 4 to 5 mg. was required for these procedures done under light pentothal-gas anesthesia. In most cases, vital reflexes returned before the patients left the operating room.

Upper abdominal surgery was usually more difficult, and surgeons more frequently complained of inadequate exposure. Deeper anesthesia was usually necessary with ether being added to the anesthetic as a supplemental or, more often, as a primary agent. Respiratory traction reflexes, such as breath-holding, were particularly bothersome in surgical procedures on the gallbladder. Excessive movement of the diaphragm after abdominal and intercostal muscles were paralyzed frequently created a bothersome motion in the operative field even though relaxation otherwise was adequate. This effect usually was short-lived and could be controlled partially by manual support of

respiration. Variability of individual response to syncurine and tachyphylaxis was particularly evident in upper abdominal operations where greater relaxation is necessary and operations are often of longer duration.

Rather profound respiratory depression was almost unavoidable in upper abdominal operations, and in fact some decrease of tidal volume was noted in the majority of patients in whom relaxation was adequate for lower abdominal work. Actual apnea occurred in a relatively small number of patients. Respiratory depression usually lasted only a few minutes, but several patients remained apneic twenty minutes, and one remained on controlled respirations forty-five minutes. We are of the opinion that, in some instances, overactive manual support of respiration can prolong an apnea that would terminate sooner with less vigorous artificial respiration.

Following the recovery of nearly normal respiratory exchange, which usually occurred quite suddenly after a few minutes of depression, breathing was usually smooth and relaxation adequate for periods up to thirty minutes. At any time during this period, however, sudden traction upon organs or peritoneum would produce "pushing," laryngeal stridor, or breath-holding, particularly if anesthesia had become too light. Often at the time of closure, an abdomen that appeared adequately relaxed for closure would become unmanageable after application of clamps to the peritoneum, and more syncurine would have to be given.

Total dosage of syncurine used for any one patient depended to a great degree on the individual tolerance of the patient. Usually, maintenance doses had less and less effect, and the original dose could be given at the end of operation without causing the respiratory depression seen originally. It has been pointed out recently that this tachyphylaxis applies only to the curarizing effect of syncurine and that we do not know whether there are other properties of the drug which are similarly affected (2). Here lies, perhaps, the explanation for some instances of prolonged apnea that have been reported in the literature (8). For this reason we recommend that the total dosage be kept low.

Endotracheal intubation was particularly facilitated by the use of syncurine, which was employed in over half the cases in this series primarily for intubation. The dose most frequently used was 2 mg., injected through the intravenous tubing immediately after induction with pentothal. Usually the patient was ready for intubation within five minutes after the injection. During this period we frequently administered oxygen or gas-oxygen as prophylaxis against hypoxia during the act of intubation. Topical cocainization just before intubation helped materially in reducing coughing and breath-holding following passage of the tube. Usually the jaw was found to be well relaxed and the vocal cords well abducted, offering an excellent laryngoscopic view. Manual support of respiration was employed routinely after

passage of the tube. Occasionally additional cocaine was applied through the endotracheal tube if coughing was excessive.

Nasal intubation was also facilitated by small amounts of syncurine. Laryngospasm from blind manipulation was largely overcome, but reduction of tidal exchange sometimes hindered placement owing to the quietness of respiration. Prior curarization, however, rendered the patient ready for visualized intubation in the event of failure of blind intubation.

No patients were given syncurine if doubt existed that intubation could be done without difficulty. For instance, in patients who had ankylosis of the jaw or who had porcelain capped teeth, other methods were employed.

Syncurine is especially advantageous for intubation when further relaxation will not be needed during surgery. The evanescent curarization permits early return of adequate respirations for long head and neck operations, plastic procedures and spinal operations.

Most of the intubations in which syncurine was used were easily performed. Those that were difficult occurred usually in patients with unrecognized anatomical changes in the pharynx or larynx. Improper positioning for laryngoscopy led some of our less experienced residents into difficulties in other cases. Serious complications following intubation were seen in 3 cases; one of postoperative laryngeal edema requiring tracheotomy and 2 of granuloma of the vocal cords requiring treatment several weeks after operation. Whether the granulomas resulted from intubation or not is, of course, open to question.

We wish to emphasize that dangerous levels of hypoxia can occur during intubation under syncurine and that the anesthetist should not become so involved in carrying out intubation that he forgets to determine whether oxygenation is adequate.

The generally favorable results with intubation prompted us to employ syncurine for other endoscopic procedures. Syncurine in conjunction with pentothal for bronchoscopy has proved, in the main, to be a satisfactory procedure. The method of administration is similar to that for intubation, except that bronchoscopy is begun when the peak effect of the syncurine has passed. Oxygen is given through the bronchoscope during the procedure; if respiratory depression is excessive, the lungs are inflated by alternately opening and closing the end of the bronchoscope with the thumb. Topical cocainization was frequently employed as a preliminary to the general anesthesic but not as a routine. The surgeons in particular were pleased by the quiet respirations and ease of introducing the bronchoscope to the extent that they now prefer to do their bronchoscopies under general rather than topical anesthesia alone. General anesthesia is certainly more pleasant for the patient. Most of the patients required less than 500 mg. of pentothal and less than 3 mg. of syncurine for the procedure. Most were reacting and

had normally deep respirations at the time the bronchoscope was withdrawn.

On two occasions, difficulties were encountered. In one patient bleeding of the larynx developed when the bronchoscope was introduced. Obstruction occurred and he became cyanotic. A cuffed endotracheal tube was inserted and oxygen given until the patient recovered. Later bronchoscopy was performed without difficulty under ether anesthesia. In a second patient violent coughing and breath-holding developed before the bronchoscope was introduced. He became cyanotic but recovered with treatment with oxygen by Kreiselman resuscitator and bronchoscopy was carried out without further incident.

In a few cases syncurine has been employed for laryngoscopic biopsies and esophagoscopies. It is probably advisable to give oxygen before laryngoscopy is performed, and the danger of bleeding from the biopsy site must be recognized. Facilities for intubation should be ready in the event of excessive bleeding. Nearly all our esophagoscopies were done under endotracheal anesthesia and were uneventful. The use of an endotracheal tube, we believe, is essential for this procedure.

In obstetrical anesthesia, we have employed syncurine both to provide muscular relaxation and to allow smaller amounts of anesthetic agents to be given (with increased amounts of oxygen). For cesarean section, anesthesia is induced with pentothal and maintained with ethylene-oxygen. Induction is delayed until the obstetrician is prepared to make the incision, and the drug (usually 2 mg.) is given immediately after the patient has lost consciousness. Little effect on the infant's early respiration is seen if the baby is born within ten minutes of the induction of anesthesia.

For vaginal delivery, the patient is anesthetized with ethylene-oxygen and about 2 mg. of syncurine is injected at the time forceps are applied (or for additional perineal relaxation when decomposition of a breech is begun). The obstetrician then finds that traction is exerted against an ever-relaxing perineum. Usually forceps rotations are facilitated, and smaller episiotomies can be employed. The anesthetist finds that fewer traction reflexes (for example, laryngeal stridor) occur under light ethylene-syncurine anesthesia than under ethylene alone.

As a rule, some effect is seen on the newborn. About half of them require resuscitation, depending on how much sedation the mother has previously had and how long the syncurine effect has been present before delivery is accomplished. Usually, the babies are more flaccid, but the flaccidity wears off quickly. Many breathe with vigorous spontaneous respirations as soon as they are born, but the delivery room personnel must be prepared to resuscitate a number of these infants. One neonatal death occurred in a premature infant delivered by cesarean section for premature separation of placenta.

Operative and postoperative deaths occurring during this two year

period were as follows: 3 in the operating room, 4 on the day of operation or on the first postoperative day, 23 others postoperatively. The cause of the three operating room deaths was as follows: (1) multiple embolization during mitral stenosis operation (release of mural thrombi), (2) ventricular fibrillation during mitral stenosis operation, and (3) coronary thrombosis during a Smithwick operation.

Only in the third case could the use of syncurine be considered as a possible contributory cause of death. Intubation had been performed with difficulty under pentothal-syncurine some forty-five minutes before the coronary occlusion occurred. During intubation the patient had become cyanotic and transient blood pressure fall had occurred. The blood pressure and pulse remained normal after the operation started until the surgeon began to resect a rib. At that time blood pressure, pulse and respirations ceased. Postmortem examination revealed a coronary thrombosis.

The four immediate postoperative deaths were as follows: (1) sudden death after craniotomy, the cause undetermined but probably due to cerebral edema, (2) coronary occlusion after the patient got out of bed on the day of operation, (3) hemorrhage and (4) cardiac failure after an aneurysm operation. There was no evidence that syncurine was in any way responsible directly or indirectly in any of these deaths. The other 23 postoperative deaths occurred up to three months after operation and were not related to anesthesia in any way.

Therefore, the entire incidence of mortality in our series was approximately 1 to 2,400. This incidence is considerably at variance with the figure of 1 to 370 given in a report by an anesthesia study commission (9) as being the incidence of death in anesthesias in which curare (all types) was used.

Atelectasis developed in 10 patients, requiring postoperative bronchoscopy. Five of the patients had had pneumonectomies or lobectomies.

Other postoperative complications were: shock, 7 cases; cyanosis, 3 cases; congestive heart failure, 2 cases; pulmonary infarct, one case, and transient amnesia due to hypoxia, one case. The cases of cyanosis and amnesia were related to respiratory depression following administration of syncurine during the surgical procedure.

PRECAUTIONS

Since respiratory depression to some degree must be expected following the administration of syncurine it should be given only under the supervision of a competent anesthesiologist. Oxygen equipment for artificial respiration should always be on hand, and manual support of respirations should be given as prophylaxis against hypoxia in most cases. Oropharyngeal airways should be employed routinely, and endotracheal equipment should be at hand for use when indicated. Effort should be made to keep the dosage of syncurine minimal.

CONCLUSIONS

Decamethonium bromide (syncurine®) has been used in 2,403 cases at George Washington University Hospital and the results are reported.

Among its properties are rapidity of action, shortness of duration, tachyphylaxis, absence of histamine activity, variability of individual reaction and depression of respiration.

Most satisfactory results were obtained in lower abdominal operations of short duration, endotracheal intubation and endoscopy. Least satisfactory results were obtained in upper abdominal operations and surgical procedures of long duration.

Syncurine is of some benefit to the obstetrician, but some effect of the drug may be seen in the newborn.

One death in the 2,403 cases may have been indirectly caused by anoxia following administration of syncurine and intubation.

Precautions are enumerated, with particular emphasis on adequate oxygenation of the patient and the use of low dosage of decamethonium bromide.

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