CLINICAL OBSERVATIONS ON THE USE OF CURARE IN ANESTHESIA

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The use of curare in conjunction with general anesthesia to improve muscular relaxation was first reported in this journal by Griffith and Johnson (1). They found that when sufficient relaxation could not be obtained with inhalation anesthesia, 100 mg. of curare (Intocostrin-Squibb) would immediately produce profound relaxation for a short time. More than 100 mg. of curare was rarely required. When it was used in conjunction with cyclopropane, undesirable reactions were not observed. Respiratory depression occasionally occurred, but was readily treated by artificial respiration and lasted only a short time.

Cullen (2) reported favorably on the use of curare and stated that the principal disadvantage of curare is the narrow margin between abdominal relaxation and respiratory depression. In many cases when sufficient curare was given to relax the abdominal muscles, a degree of respiratory paralysis occurred that required artificial pulmonary ventilation. Cullen noted that when curare was used with ether anesthesia, it was necessary to reduce the dose of curare. Our experience with curare during ether anesthesia has been similar to that of Cullen. We have found that 20 mg. doses of curare improve the relaxation of first plane ether anesthesia while large doses, 100 mg. or more, may precipitate severe circulatory depression. In the presence of deep ether anesthesia, even small doses of curare may cause severe circulatory reactions. The intravenous injection of 20 mg. of curare in one patient in the third plane of ether anesthesia caused complete peripheral circulatory failure. The circulation was restored by promptly decreasing the depth of inhalation anesthesia. Another patient was given 20 mg. of curare following the administration of 400 cc. of a 5 per cent solution of ether intravenously. Immediately following the injection of curare the peripheral pulse could not be detected and the patient required very active resuscitative measures before recovery occurred. Other similar experiences with ether and curare have emphasized the necessity of exercising considerable caution when these two agents are used together. If sufficient ether has been given to produce third plane anesthesia and the relaxation is still unsatisfactory, it is probably unwise to use curare.

We have used curare for the most part to supplement cyclopropane.

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anesthesia. Circulatory depression was not observed with this combination if the patients were well oxygenated at all times. When it was necessary to obtain muscular relaxation very quickly, 100 mg. of curare was given intravenously. This promptly provided good relaxation in most cases; however, varying degrees of respiratory depression occurred which often required artificial respiration. It was usually not necessary to decrease the depth of cyclopropane unless an excessive amount had been given prior to the administration of curare. If the anesthesia is permitted to become too light at this time muscular spasms may occur. This complication will be discussed in another part of the paper. When adequate relaxation was once obtained, additional doses of 20 mg. were given as required. In the average case the need for additional muscular relaxation can be anticipated and the curare can be given in divided doses. When more time was available for the production of relaxation an initial dose of 20 mg. of curare was given immediately after the induction with cyclopropane, and then repeated every five minutes until the desired degree of muscular paralysis was obtained. The depth of cyclopropane anesthesia was maintained in the lower part of the first plane. The incidence of complications was minimized by the administration of curare in small divided doses and by limiting the total quantity to 100 to 150 mg.

When sufficient curare is given to paralyze the muscles of the larynx, foreign material may be aspirated into the lungs unless definite precautions, such as the use of an endotracheal tube, are taken. The following case illustrates what may happen when regurgitation occurs after the administration of a relatively large dose of curare. Four days following a gastric resection a patient was returned to surgery for relief of intestinal obstruction. The general condition of the patient was poor and the abdomen was distended. After induction with cyclopropane, a total of 160 mg. of curare was given in divided doses over a fifty-minute period. During the last fifteen minutes of this time it was necessary to maintain artificial respiration by intermittent pressure on the breathing bag. When the peritoneum was being closed the patient suddenly regurgitated a large amount of stomach contents and became very cyanotic. Although pharyngeal and endotracheal aspiration were promptly instituted the patient never regained a good color. Administration of 100 per cent oxygen did not materially decrease the degree of cyanosis. The patient gradually became worse and died two hours after the operation. The use of an endotracheal tube in this case would undoubtedly have prevented the aspiration of vomitus. The advisability of using an endotracheal tube should always be considered when curare is given to patients who are likely to vomit or regurgitate stomach contents.

Curare was used alone or in conjunction with local anesthesia in several patients. Some of these cases were briefly discussed in another paper (3). In one patient an emergency cesarean section was per-
formed on a 32-year-old female, weighing 150 pounds. The patient was exsanguinated and in severe shock due to hemorrhage from premature separation of the placenta. The blood pressure was 75 mm. systolic and 60 mm. diastolic and the pulse rate was 160. No premedication was given. The operation was started under local anesthesia but the patient was so restless that it was impossible for the surgeon to continue. Sixty milligrams of curare intravenously caused complete respiratory arrest. Artificial respiration was instituted by making intermittent pressure on the breathing bag of the gas machine. At this time marked salivation of tough, tenacious mucus occurred. This was followed by muscular spasms and twitchings, particularly of the upper extremities and head. Four minutes after the first injection of curare, 40 mg. more was given. This caused complete muscular paralysis and loss of consciousness. The duration of complete respiratory paralysis was ten minutes. It is interesting to note that the patient did not regain consciousness until fifteen minutes after she had started to breathe. Whole blood and plasma transfusions were given during the operation, which improved the circulation as indicated by a decrease of the pulse rate to 140 and an increase of blood pressure to 120 mm. systolic and 90 mm. diastolic.

Another patient was operated upon for gastric resection for uncontrollable gastric hemorrhage. The patient was 52 years old and weighed 180 pounds. At the time of the operation the hemoglobin was less than 20 per cent, red blood count was 760,000, blood pressure was 90 mm. systolic and 60 mm. diastolic, and the pulse rate was 120. Atropine, grain 1/150 (0.00043 Gm.) was given thirty minutes before operation. Blood was administered throughout the course of the operation. The line of incision was infiltrated with procaine 1 per cent and the operation was started. At the same time curare was given in 20 mg. doses intravenously at three to five minute intervals and oxygen was administered from a gas machine. At first the patient complained of considerable pain and discomfort but at the end of one hour, after 200 mg. of curare had been given, respiratory arrest occurred and consciousness was lost. During the second hour of the operation an additional amount of only 70 mg. of curare was required to maintain unconsciousness and complete muscular relaxation. The blood pressure was maintained at 120 mm. systolic and 80 mm. diastolic and the pulse rate at 120 throughout the course of the operation. Twenty minutes after the operation was completed the patient regained consciousness and the respiratory activity became adequate. A total of 270 mg. of curare was used. The abdominal relaxation was excellent and there was no evidence of circulatory depression due to the curare.

When sufficient curare was given to cause complete paralysis of all the skeletal muscles, an abrupt loss of consciousness occurred without any preceding period of analgesia. There was no clinical evidence of hypoxia when unconsciousness occurred in these cases. At another
time, curare unsupplemented by other agents was administered to a 72-year-old white female, weighing 145 pounds, for a resection of the colon. This patient was alert and in fairly good physical condition. The premedication consisted of morphine sulfate grain $\frac{1}{8}$ (.008 Gm.) and atropine sulfate grain $\frac{1}{150}$ (.00043 Gm.) one hour preoperatively. An initial dose of 125 mg. of curare intravenously caused complete respiratory arrest and immediate loss of consciousness. Artificial respiration was instituted and readily maintained due to the profound muscular relaxation. Additional amounts of curare in 20 to 40 mg. doses were given at ten to fifteen minute intervals throughout the operation. After the first dose of curare the patient had an active corneal reflex but this disappeared when a total of 225 mg. of curare was given. The blood pressure increased from 150 mm. systolic and 90 mm. diastolic to 190 mm. systolic and 110 mm. diastolic, and the pulse rate dropped from 96 to 72. The circulation was so maintained throughout the course of the operation, which lasted one hour and forty-five minutes. Additional doses of curare were administered whenever muscular activity started to return. This was indicated by increased resistance to manual inflation of the lungs. A total of 405 mg. of curare was given to maintain unconsciousness and complete relaxation. Although respiratory effort started at the end of the operation, the effect of the curare did not wear off sufficiently to permit adequate respiration until four hours after the operation had been completed. In this case respiratory activity started forty-five minutes before the patient regained consciousness. During the period of postoperative respiratory depression it was necessary to maintain artificial respiration. The prolonged respiratory depression that may result from the use of large amounts of curare increases the danger of postoperative complications. The administration of curare in this manner has not been sufficiently satisfactory in our experience to warrant its extended use.

In two patients an attempt was made to produce analgesia by administering repeated small doses of the drug. Sufficient curare was given to cause marked but not complete respiratory paralysis. Although these patients could not move they showed evidence of pain as soon as the operation was started. After a short time they were anesthetized with cyclopropane. Postoperatively both patients vividly remembered everything that occurred prior to the induction with cyclopropane. They stated that the pain was unbearable before the anesthesia was started.

West (4) has called attention to the occurrence and danger of respiratory spasms during the administration of curare. We have noted this complication in several cases when inadequate general anesthesia was used and when the amount of curare was insufficient to cause complete paralysis of the skeletal muscles. A white woman, scheduled for pelvic laparotomy, was lightly anesthetized with cyclo-
propane. One hundred milligrams of curare was given intravenously, which promptly caused respiratory arrest. Artificial respiration was instituted and the depth of inhalation anesthesia was decreased by emptying the breathing bag several times and filling it with oxygen. For a period of fifteen minutes after the curare was injected, the lungs were easily inflated and the circulation was not affected. The operation was started during this time and the relaxation was complete. Suddenly it became increasingly difficult to inflate the lungs because of spasms of the muscles of respiration. There seemed to be a definite bronchospasm which prevented pulmonary ventilation. This was followed by a rapid fall of blood pressure and a decrease of the pulse rate from 88 to 32 per minute. Operative manipulation was temporarily suspended and 15 mg. of ephedrine was injected intravenously. This restored the circulation and permitted better oxygenation of the patient. Cyclopropane was then administered to prevent reflex stimulation, and the operation progressed without further difficulty. This case illustrates what may occur when curare is used without adequate inhalation anesthesia.

Another patient, very lightly anesthetized with cyclopropane, was given an initial dose of 180 mg. of curare intravenously. Complete paralysis immediately occurred and an intra-abdominal operation was started which progressed satisfactorily for a period of fifteen minutes. During this time the circulation was unaffected. It then became increasingly difficult to inflate the lungs and the blood pressure started to fall. At this time an additional 100 mg. of curare was given. Immediately following this, the lungs could be readily inflated and the blood pressure returned to its previous level, indicating that the cause of the circulatory depression was probably hypoxia rather than a direct effect of the curare. The administration of curare to overcome respiratory spasm has been done repeatedly with satisfactory results. After the muscles are relaxed by the curare, additional inhalation anesthesia can be given to obtain the proper level of anesthesia.

When respiratory spasms occur, it is necessary either to increase the depth of anesthesia, or to give additional curare to relax the muscles and permit inflation of the lungs. If the muscles of respiration are not relaxed, attempting to inflate the lungs may force gas into the stomach. This results in a dilated stomach which may embarrass the work of the surgeon. Forceful distention of the stomach may also cause an unexpected regurgitation of stomach contents. The danger of pulmonary aspiration after the use of curare has already been discussed. When the dose of curare is limited and when the general anesthesia is adequate, muscular spasms have not been observed. Muscular twitchings and spasms are sometimes observed during the recovery period following the administration of large doses of curare. In the absence of operative stimulation the bronchospasms are usually not severe and can be readily overcome by artificial respiration.
USE OF CURARE IN ANESTHESIA

We have used curare with very satisfactory results in conjunction with spinal-cyclopropane anesthesia to improve or prolong abdominal relaxation. When the relaxation is grossly unsatisfactory, 100 mg. of curare intravenously will promptly improve the relaxation without causing circulatory depression. Ordinarily, whenever there is evidence of inadequate spinal anesthesia, or when it is wearing off too soon, 20 mg. doses of curare are given and then repeated every five minutes until the desired effect is obtained. The use of curare in this fashion has decreased the necessity of using the continuous spinal technic in many of our cases.

Curare has been used in conjunction with cyclopropane anesthesia for cesarean sections in 100 cases with satisfactory results. Curare does not seem to exert a depressing effect on the baby and it definitely decreases the amount of inhalation anesthesia required. The curare is administered in 20 mg. doses and repeated every three to five minutes until there is beginning evidence of respiratory depression. A total of 100 mg. of curare is used in the average case. The first injection of curare is given before the patient is anesthetized with cyclopropane and an attempt is made to use as little cyclopropane as possible until after the baby is delivered. In no instance has a baby been severely depressed, but slight depression has been encountered more frequently than with spinal or local anesthesia. At the present time it is our impression that this combination warrants further trial.

CONCLUSION

In our experience curare has not displaced the ordinary methods of producing relaxation for routine intra-abdominal operations. The conservative use of curare as a method of improving relaxation, particularly when used in conjunction with cyclopropane, has been advantageous in some instances. The combination of curare and cyclopropane causes very little circulatory depression even in poor risk patients if they are well oxygenated at all times. Although many patients tolerate relatively large doses of curare, we have observed fewer complications when it is given in small divided doses and when the total quantity of drug is limited to 100 to 150 mg. In the average case, doses of 20 mg., repeated at five minute intervals until the desired effect is obtained, have been a satisfactory method of administering curare.

When large doses of curare were used certain complications were observed. Prolonged paralysis of the muscles of respiration and muscular spasms frequently occurred, which often caused hypoxia. Thick, tenacious mucus accumulated in the mouth and pharynx. This caused the patient considerable annoyance during the postoperative period. The pharyngeal and laryngeal reflexes are less active following the administration of large amounts of curare. This increased the danger of aspirating foreign material. The use of curare often necessitated
artificial respiration. Occasionally this would result in distention of
the stomach which would sometimes interfere with the operation.
Serious circulatory depression was very prone to occur when curare
was given to patients in deep ether anesthesia; consequently, the
combination of curare and ether has been abandoned unless the patient
is in a very light plane of ether anesthesia.

Analgesia was not obtained with curare; however, large doses
did produce complete relaxation of the skeletal muscles and un-
consciousness. It does not seem advisable to administer sufficient
curare to produce this effect for surgical operations. Since some
degree of respiratory depression usually accompanies the administra-
tion of curare, every effort should be made to prevent hypoxia and the
retention of carbon dioxide.

The introduction of curare into clinical anesthesia is another step
in the progress of anesthesiology. Sufficient experience is not available
as yet to outline clearly its true scope of usefulness or to delineate
sharply its limitations. At the present time there is reason to believe
that the cautious use of curare in conjunction with other agents will
prove to be valuable in selected cases.

REFERENCES

1. Griffith, H. R., and Johnson, Enid: The Use of Curare in General Anesthesia, Anesthesiology
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2. Cullen, S. C.: Clinical and Laboratory Observations on the Use of Curare During Inhalation
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COMING EXAMINATIONS

The Annual Meeting of the American Board of Anesthesiology,
Inc., will be held at the Waldorf-Astoria, New York, N. Y., June
13, and the Oral Examinations, June 14 to 17, 1945. Secretary:
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