THE USE OF OXYMORPHONE HYDROCHLORIDE* DURING ANESTHESIA FOR OPERATIONS ON THE HEAD AND NECK

A Preliminary Report

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THIS paper is a brief report of our experience in the use of oxymorphone hydrochloride during anesthesia for surgical procedures involving the head and neck. Operations for cancer and procedures for cosmetic repair such as nasoplasty and septal reconstruction are included. No particular originality is claimed in respect to the technic described in this paper. We have found this technic to be safe for the patient and to be satisfactory to the surgeon in providing good operating conditions. It is believed that oxymorphone may well prove to be adaptable to operations involving not only the head and neck, but also other parts of the body.‡

The new synthetic, morphine-like alkaloid, 14-hydroxydihydromorphinone, has shown high analgesic potency on the basis of experimental and clinical investigation.[1] *Figure 1* shows the structural relationship between oxymorphone, morphine, and dihydromorphinone. Oxymorphone differs from morphine by the replacement of an alcoholic hydroxyl group by an oxygen atom at carbon 6 position, and attachment of a hydroxyl group at the fourteenth position, and from dihydromorphinone by a hydroxyl group in the fourteenth position.[2] The 7-8 bond is saturated in oxymorphone and unsaturated in morphine and dihydromorphinone.

The analgesic potency of oxymorphone in mice has been studied by Samuels, Stehlin, Dale, and Howe[3] using the hot-plate method of Eddy and Limbach injecting the drug subcutaneously. Oxymorphone was found to be 15 times as active as morphine and 2.5 times as active as dihydromorphinone.

In clinical studies Eddy and Lee[4] have shown that 2 mg. of oxymorphone is equivalent to 16 mg. of morphine sulfate, to 100 mg. of meperidine hydrochloride, or to 5 mg. dihydromorphinone. Respiratory depression appeared to be the most serious toxic symptom, but usually was minimal in patients who were not debilitated who received individual doses of no more than 5 mg. Nalorphine hydrochloride will rapidly counteract respiratory depression induced by oxymorphone.

The anesthesiologist must plan his technic so that the anesthesia is as light as feasible to allow prompt recovery even after long procedures. The technic must

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‡Subsequent to the series reported in this paper, oxymorphone was employed with great efficiency in thoracic operations.

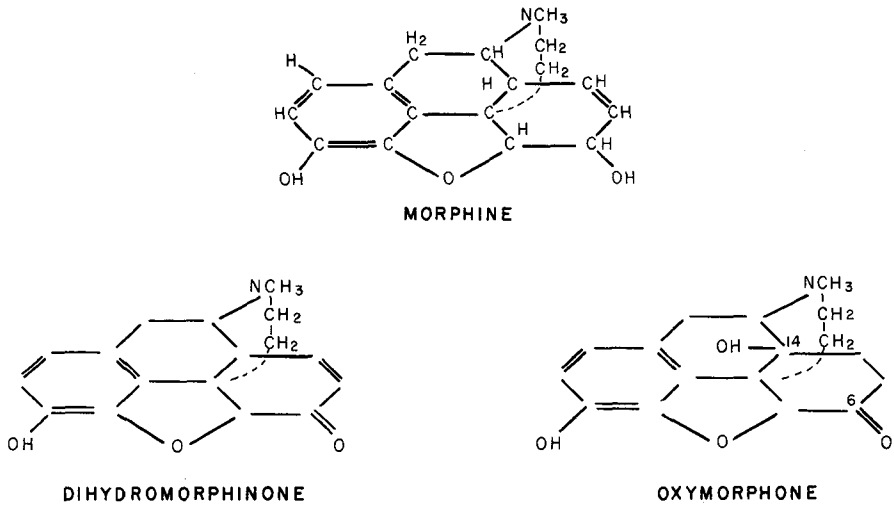

Fig. 1. Comparison of chemical structures of three anesthetic agents: morphine, dihydromorphinone, and oxymorphone.

not contribute to the deterioration of already existing pulmonary insufficiency. The aim of the anesthesiologist is to send the patient to the recovery room in possession of reflexes that will enable him to cope with blood and mucus in the trachea. This is of vital importance in patients who do not have a tracheotomy when an extensive surgical procedure and massive bandaging of the head and neck interfere with the airway.

In patients with neoplasm of the head and neck, the anesthesiologist preoperatively should acquaint himself with its locality and extent, and assess the amount of respiratory obstruction. He should study the roentgenograms and ascertain whether tracheal deviation is present.

The anesthetic agents selected should allow the patient to be asleep and free from pain. The respirations should be quiet, but the cough reflex and voluntary control of respiration must be retained. Since requirements for muscular relaxations are minimal, the use of relaxant drugs is limited.

Technic of Administration

Intravenous administration of anesthetics in a patient who has severe respiratory obstruction is extremely hazardous. In such a patient, a preliminary tracheotomy under local anesthesia is an essential precautionary measure. In suitable patients, the thiopental sodium—succinylcholine—oxygen sequence is employed prior to endotracheal intubation.

Premedication. In healthy adult patients, the usual premedication consisted of meperidine hydrochloride, 50 or 100 mg., and atropine sulfate, 0.6 mg. (1/100 gr.).

In extremely sick patients, only atropine sulfate was used. It is essential that atropine be used to protect the patient against the vagal stimuli resulting from surgical manipulation of the carotid sinus. In patients who have tachycardia, scopolamine, 0.5 mg. (1/150 gr.), may be substituted for atropine.

Anesthesia. Hypnosis was induced by 2 per cent solution of thiopental sodium, and initial muscular relaxation was provided by succinylcholine chloride, 50 mg., injected intravenously. The patient was given manual respiration with 100 per cent oxygen, and a cuffed endotracheal tube was inserted into the trachea. Maintenance of anesthesia was then provided by inhalation of a mixture of nitrous oxide and oxygen, of which 25 to 30 per cent was oxygen.

Adequate basal analgesia was provided by the intravenous injection of oxymorphone supplemented by inhalation of nitrous oxide and oxygen. The initial dose of oxymorphone was from 0.375 to 0.75 mg.; this amount was supplemented by additional doses of 0.375 mg. as required.

Results

In our series of 50 operations upon the head and neck, the outlined anesthetic technic produced good surgical operating conditions. The analgesia was profound and the patient could withstand the most powerful stimuli without showing signs of being disturbed. In spite of the severity of the surgical procedure and massive bandages, the patient maintained his airway and spontaneous breathing. In addition, he was tranquil and free of pain, the state characteristically induced by oxymorphone. At the conclusion of the operation, each patient was awake and in control of his vital protective reflexes; he was easily aroused, and, when requested, coughed.

Side effects. The side effects after intravenous injections of oxymorphone varied with the individual patient, and involved decrease in blood pressure and depressed respiration. In some patients there was an initial fall in systolic blood pressure of as much as 20 mm. of Hg. The decrease in blood pressure was never severe and in most patients was corrected spontaneously; an intravenous injection of a 5-mg. dose of methoxymine hydrochloride* restored normal blood pressure in the others.

The respiratory rate often was depressed, in some instances falling to as low as four respirations per minute. At that stage, respiration was assisted manually. When the rate is at 12 respirations per minute, ventilation is adequate, as the depth of respiration seems to be increased with oxymorphone. There was no clinical evidence of overaccumulation of carbon dioxide. At the end of the operation, if the respiratory rate was inadequate, an intravenous injection of nalorphine hydrochloride, ½ to 1 ml. (2.5 to 5 mg.), brought about an immediate response to normal.

No histamine reactions were observed.

*'Vasoxyl,' Burroughs Wellcome & Co. (U.S.A.) Inc.

Discussion

"Balanced anesthesia," a term coined by Lundy,[5] has been used extensively to designate the triad of the state of anesthesia—amnesia, analgesia, and relaxation. In the years when diethyl ether was the sole anesthetic agent used, all the individual prerequisites of anesthesia were supplied by the single agent. With the advent of thiopental sodium, the amnesia it produced could be supplemented by analgesic agents such as nitrous oxide, halothane, or cyclopropane. Relaxation was produced by curare derivatives or succinycholine chloride, but all the anesthetic superstructure was built on a foundation of narcotic premedication. In many departments of anesthesiology the policy is to use minimal premedication. Now it becomes necessary for the anesthesiologist to supplement the premedication by the intravenous injection of an additional narcotic. In trials of various narcotics, the useful effects of oxymorphone were discovered.

Numerous technics using various agents were attempted before the method described was evolved. Early in this study, halothane and divided doses of meperidine were employed to provide general anesthesia (amnesia and analgesia). Halothane was particularly useful, as it causes bronchodilatation. It was the preferred agent in those patients with respiratory disease, but the use of epinephrine by the surgeon incurred the possibility of inducing aberrant myocardial rhythms, and necessitated a revision of the anesthetic technic. Although halothane offers ideal analgesic qualities for surgical procedures on the head and neck, it has the one great disadvantage of sensitizing the heart to epinephrine. The inhalation of halothane, therefore, in our series was replaced by inhalation of nitrous oxide and oxygen. To supply sufficient analgesia with the nitrous oxide—oxygen technic, additional basal narcosis was required. Meperidine as a supplement was ineffective, and in adequate doses produced hypotension. In view of this experience it was decided to assess the value of oxymorphone.

It was immediately evident that when oxymorphone was administered during anesthesia, it produced a profound analgesic effect. In fact, the effect was much greater than that produced in a patient not under general anesthesia. For this reason, we are led to believe there is a synergistic effect between the oxymorphone and the nitrous oxide, thiopental sodium, or a combination of nitrous oxide and thiopental sodium. The amount of oxymorphone for basal narcosis must be reduced as compared to the amount administered in the preoperative and postoperative periods. The patient's respiratory excursions now are easily controlled. This is a great advantage when inducing anesthesia for head and neck operations; the patient must not cough or strain.

The synergism with the other anesthetic agents may also cause the decline in respiratory rate. However, associated with this reduction is an increase in tidal volume. Spontaneous respiratory excursions during such surgical procedures are supported by manual compression of the breathing bag or by an artificial respirator. When necessary, the respiratory rate may be returned to normal by the intra-

venous injection of nalorphine, as mentioned.

In some patients the blood pressure was so altered as to cause a hypotension in the range of 10 to 20 mg. of Hg. This range in most cases is within the normal physiologic bounds. It contrasts greatly with the circulatory depression experienced with the administration of meperidine, after which the blood pressure often verges on levels of shock. The hypotension caused by oxymorphone can be rapidly reversed, if necessary, by the administration of any vasopressor.

Summary

The problems in anesthetizing patients who are to undergo operations on the head and neck include coping with already existing pulmonary insufficiency; and keeping the anesthesia as light as feasible to allow prompt recovery after long surgical procedures. Oxymorphone hydrochloride has given profound analgesia, and good operating conditions for the surgeon in a series of 50 patients. The drug was safe as well as effective. Unlike other narcotic agents, oxymorphone does not produce deep hypnosis, but rather a state of profound tranquility and freedom from pain. The patient may be aroused easily and controls all his vital reflexes.

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