THE USE OF HYALURONIDASE WITH TOPICAL ANESTHESIA FOR ENDOTRACHEAL INTUBATION * † ‡

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TOPICAL anesthesia of the respiratory tract is an important tool for endoscopic examinations and has become increasingly popular for the facilitation of endotracheal intubation. The widespread employment of anesthetic agents on respiratory mucous membranes has served to emphasize the dangers of rapid absorption from these mucosal surfaces (1). Severe drug reactions in the form of convulsions and circulatory collapse are not rare (2, 3). However, there seems to be reasonably good evidence that harmful sequelae are related to the quantity and rapidity of absorption of drug rather than to idiosyncrasy to small amounts of anesthetic agent. The nebulizing technics described by Miller et al. undoubtedly accomplish the purpose of effective anesthesia with small quantities of drug, but much time (thirty to forty minutes) is consumed in the process (4).

The use of hyaluronidase in this connection was suggested by the experiences of others in related problems (5, 6, 7, 8). Furthermore, it is reasonable to expect that the mucolytic properties of the enzyme can be exploited to advantage in permitting more rapid anesthetic action to take place on surfaces of mucous membranes with less drug if the overlying mucous coating were removed. If this assumption is correct, topical anesthesia can be achieved more rapidly with less anesthetic agent by the addition of hyaluronidase. Hyaluronidase is safe for clinical use in that no adverse effects, either systemic or local, have been observed.

METHODS

Hyaluronidase was employed by the addition of 10 turbidity reducing units (TRU) to each cubic centimeter of 2 per cent pontocaine solu-

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tion. Preliminary experiments were conducted upon 20 healthy volunteers in an effort to ascertain the time of onset of surface anesthesia of the tongue when the pontocaine-hyaluronidase solution was compared to pontocaine alone. The results were definitive in that hyaluronidase shortened the time required for the onset of anesthesia by approximately 45 per cent. Observations on the duration and pattern of anesthesia were less decisive and could not be determined with reasonable precision.

After this preliminary experience, 125 patients were studied who were scheduled for neurosurgical operative treatment during endotracheal anesthesia with pentothal and nitrous oxide-oxygen. All patients were in relatively good health other than the specific lesion requiring surgical intervention. Respiratory activity and mental alertness were normal; there were no comatose or semicomatose patients in the study. Cases meeting these requirements were selected at random in other respects. Topical anesthesia was completed with a standardized method consisting of the application of anesthetic drug to certain and constant areas of the mouth, pharynx and larynx. Anesthesia was effected only in the structures which are contacted by the laryngoscope blade. Preliminary experience indicated that only the base of the tongue and hypopharynx required anesthesia for efficient visualization of the glottis. The base of the tongue was anesthetized by an ordinary De Vilbiss atomizer on the first spray. The laryngoscope was then introduced and, if tolerated, the glottis was sprayed, but if not tolerated, the hypopharynx itself was sprayed. In this procedure no attempt was made to anesthetize the lips, tip of the tongue, hard palate, uvula, or tonsils directly. After the glottis had been sprayed once, the laryngoscope was again introduced and if the vocal cords were not moving, a laryngeal cannula was introduced between them into the trachea. If the vocal cords were active, they were sprayed again and the laryngeal cannula was used when subsequent visualizations showed the vocal cords to be immobile. In the early cases it soon became apparent that patients could tolerate 0.5 cc. of the agent when instilled by the laryngeal cannula with a minimum of coughing. The instillation of amounts of 1 cc. or more, however, results, in most cases, in severe coughing and bronchospasm with resultant cyanosis. Therefore, in this series the drugs were instilled in 0.5 cc. quantities.

The end point of anesthetization was determined in the following manner. After the initial 0.5 cc. instillation into the trachea, the patient was observed for cough subsequent to succeeding instillations. If any instillation, be it second, third or so forth, elicited no cough, the patient was immediately intubated and observed for a reaction to the tube. The onset of topical anesthesia under these conditions was considered as that situation in which neither cough nor reaction on the endotracheal tube was noted. Sodium pentothal (0.1 to 0.25 gm.)

was administered intravenously at the time of intubation. It is thought that the use of this drug in this manner did not interfere with the interpretation of the quality of topical anesthesia since it regularly provokes coughing or straining during intubation if topical anesthesia is inadequate.

RESULTS

A summary is given in table 1 of the quantity of topical anesthetic agent required for satisfactory anesthesia as previously defined. In addition, 25 patients were anesthetized with 10 per cent cocaine by the

TABLE 1

A COMPARISON OF THE TOPICAL ANESTHETIC EFFECTS OF 2 PER CENT PONTOCAINE, 2 PER CENT PONTOCAINE-HYALURONIDASE AND 10 PER CENT COCAINE ON THE RESPIRATORY TRACT

Agent	No. of Cases	Average Dose		Range, mg.	Time for Intubation; minutes
		cc.	mg.		
2% Pontocaine (Control)	50	4.75	95	80–180	14
2% Pontocaine-Hyaluronidase	50	1.90	39	30–100	9
10% Cocaine	25	1.60	160	120–300	7

standard technic. These are summarized as well. It is clear that the addition of hyaluronidase reduces the average dose of pontocaine for the production of satisfactory topical anesthesia to 40 per cent of the control. The data in table 1 also indicate that anesthesia is effected more rapidly when hyaluronidase is added to the 2 per cent pontocaine solution.

Further analysis of the data shows that 47 of the 50 patients anesthetized with 2 per cent pontocaine-hyaluronidase solution required less than 3 cc. of the agent, whereas only 6 of the 50 studied for whom 2 per cent pontocaine solution was used could be anesthetized with the same quantity of drugs. The remaining 44 patients required more than 4 cc. of 2 per cent pontocaine solution. Similarly, 49 patients anesthetized with 2 per cent pontocaine-hyaluronidase solution required less than ten minutes for intubation, while 42 patients with 2 per cent pontocaine solution alone required more than eleven minutes.

No data are available as to the comparative duration of anesthesia, but it is fair to presume that the duration of anesthesia with hyaluronidase may not be as long as with the pontocaine solution (7). The data collected with the use of 10 per cent cocaine are included largely to point out that effective anesthesia for the purpose of intubating the trachea can be accomplished with as little as 1.6 cc. of this solution. There is no intention of comparing these findings with those when

pontocaine and pontocaine-hyaluronidase solutions are employed. No untoward reactions attributable to the topical anesthetic agents were observed in this small series.

COMMENT

The clinical evidence obtained in this study indicates that hyaluronidase added to 2 per cent pontocaine shortens the time required for the onset of topical anesthesia in the respiratory tract and also decreases the total dose to a significant degree. The question, is the economy of drug and time to obtain anesthesia of value in reducing untoward topical drug reactions, cannot be answered directly from the observations reported since no such complications were recognized in either control or experimental group. It is not unreasonable to make this assumption, however, since drug reactions are related to the rapidity and quantity of drug absorbed. The less drug used, the lower should be the incidence of unfavorable effects in larger series of observations.

The mechanism by which hyaluronidase achieves the effects which were observed is open to speculation. It is suggested, as a possible explanation, that the ease of onset of anesthesia with smaller anesthetic doses may be associated with the dissolution of mucus by hyaluronidase, thus exposing the mucosal surfaces more readily to the action of the topical anesthetic agent. Further corroboration of this assumption is based upon other observations of patients with excessive quantities of secretions from the respiratory tract resulting from disease of the central nervous system or pulmonary disease. In these patients satisfactory topical anesthesia with 2 per cent pontocaine requires three times the time and dose that is necessary with 2 per cent pontocaine-hyaluronidase mixtures.

SUMMARY

Hyaluronidase (10 turbidity reducing units per cubic centimeter) added to 2 per cent pontocaine solution is useful in reducing the effective anesthetic dose and time of onset of anesthesia in the respiratory tract. The probable mechanism of action is described.

It is suggested that the reduction of dose of pontocaine in this manner may be an increased safety factor in topical anesthesia.

A simple method for obtaining good topical anesthesia of the larynx and trachea is described.

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