

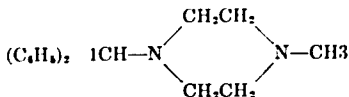
## TREATMENT OF POSTOPERATIVE VOMITING\*

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THE problem of postoperative vomiting is not a vexing one in the private practice of anesthesia, nor in the postoperative care of patients in a hospital that does not maintain a recovery room. In an institution with a recovery room, it immediately becomes apparent that if 15 or 20 patients per day are admitted, the care of many patients with postoperative vomiting is a problem. If one sees 5 or more patients in the throes of severe vomiting at the same time, it is sufficient to warrant a determined attempt to decrease this incidence. Accordingly, the following study was undertaken—the drug employed in this investigation was ‘marezine’ brand cyclizine lactate. It has been investigated in oral form by Chinn (1) *et al.*, but not in the injectable form which was supplied to us by the makers. This was wholly a recovery room study and the patients were under observation in the immediate postoperative period until returned to their wards.

Chemically, the drug is N-benzhydryl-N'-methyl piperazine with a molecular weight of 266 and a melting point of 106 to 109 C. The formula is as follows:



It is a white, crystalline solid, soluble in alcohol and chloroform, and slightly soluble in water. It has an atropine-like action and an anti-histaminic-like action.

The parasympathetic action of this agent is shown by the fact that in the cat it blocks the fall in blood pressure that results from stimulation of the right vagus nerve. This action is accomplished by twenty times the dose of atropine necessary to produce the same effect. The block is peripheral to the site of stimulation since stimulation of the central end of the vagus renders an unaltered response. It appears to act specifically on the parasympathetic ganglia as the action of injected acetylcholine on the parasympathetic nerve endings is unchanged. Feldberg (2) investigated the antispasmodic action and showed further evidence

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of this parasympathetic ganglionic blocking activity. In the isolated ileum of the guinea pig it blocks the spasmogenic action of acetylcholine and reduces the tonus and rhythmic contractions of the intestine. This activity is about 0.85 per cent that of atropine.

The antihistaminic action of marezine® is fairly potent and was determined by its ability to prevent or reduce the severity of bronchoconstriction in guinea pigs exposed to nebulized histamine. The compound also appears to have moderate local anesthetic activity.

The LD<sub>50</sub> in albino mice was 87 mg. per kilogram when given intraperitoneally. Symptoms in the fatal range were nervousness, increased activity and initial respiratory stimulation. Death was preceded by coma and dyspnea. In a study of chronic toxicity the red cell count, the white cell count and the differential count were found to be well within the normal range. The gastrointestinal tract, lungs, kidneys and liver in the sacrificed animals were within normal limits. There was no mortality and no evidence of chronic toxicity in the experimental animal in the group studies.

This drug was tested against motion sickness on troop transports in 1952 and again in 1953 by Chinn (1, 3) and was found to afford significant protection without untoward effects.

In view of the previous reports by Moore (4) and Rubin (5) on the use of similar drugs to control postoperative vomiting, the following investigation was undertaken to ascertain the value of marezine with respect to postoperative vomiting. The status of 1,000 consecutive patients who were admitted to the recovery room was carefully evaluated for the occurrence of vomiting in the immediate postoperative period. These patients were entirely unselected as to surgical procedure, premedication or anesthesia. It is pertinent to mention here the fact that those patients undergoing minor surgical or biopsy procedures under local anesthesia were not brought to the recovery room. The patients had undergone all types of operations except neurosurgical procedures, tonsillectomies and adenoidectomies; obstetrical patients and the great majority of gynecological patients also were excluded. The patients in this last named group are operated upon in another section of the institution and therefore are not brought to the recovery room.

After this initial survey, the incidence of postoperative vomiting was determined in 100 consecutive patients who were given any type of general anesthesia and 100 consecutive patients who received only spinal anesthesia. Marezine was administered therapeutically to approximately 50 per cent of those patients who exhibited one or more episodes of postoperative vomiting in the recovery room. The dosage employed was 50 mg. for adults and 25 mg. for children, and the drug was injected in the deep subcutaneous tissue. Following these studies, 100 consecutive patients who received any form of general anesthesia, and 100 consecutive patients who received only spinal anesthesia were given marezine prophylactically. The prophylactic dose employed was the same

as the therapeutic dose, 50 mg. in the adult and 25 mg. in children, administered in the deep subcutaneous tissue. In the prophylactic study the drug was given approximately thirty minutes before the expected termination of the operation. The area of injection was circled with tincture of zephiran<sup>®</sup> so that the site of injection could be evaluated.

### RESULTS

The over-all incidence of postoperative vomiting in this study of 1,000 consecutive cases is 21.3 per cent. This figure seems slightly lower than that reported in similar studies and two factors may be responsible for this relatively low incidence. First, the exclusion of minor surgical procedures and the types of operation mentioned previously may have reduced the over-all incidence. Second, it is probable that the incidence of vomiting would have been much higher if all patients were followed for a period of twenty-four to thirty-six hours; however, since we were interested in results in the immediate postoperative period we thought that if there were any significant change in this incidence it would be apparent in the time during which these patients were under observation in the recovery room. The length of time the patients spent under direct observation varied from three to ten hours.

Marezine was given therapeutically to 122 patients. Of this group, 93 patients had no further episodes of postoperative vomiting. Of the 29 patients who continued to vomit, 18 had general anesthesia in some form and 11 had spinal anesthesia only.

Of 100 consecutive patients anesthetized with some type of general anesthetic, and who had not received marezine, the incidence of vomiting was 19 per cent and of 100 consecutive patients who received spinal anesthesia the incidence of vomiting was 18 per cent; the incidence in the combined group was 18.5 per cent. This is within range of the anesthesia evaluation of an over-all incidence of 21.3 per cent.

In the group treated prophylactically, the incidence in 100 cases in which general anesthesia was employed was reduced to 11 per cent and in the group in which spinal anesthesia was given it was reduced to 9 per cent.

Of the 322 patients who received this drug there were no discernible untoward effects as far as could be determined, and there were no demonstrable changes in pulse, blood pressure, respiration or general condition. One patient complained of burning on injection and one patient treated outside this hospital, and not included in this group, had an area of local redness and swelling.

### DISCUSSION

In regard to the mechanism of action, Chinn *et al.* (1, 3) stated "Although certain antihistaminic drugs exert considerable protection, prophylaxis against motion sickness does not depend upon the antihista-

minic action of the drug." They further suggested that the effectiveness of these drugs must be attributed to other pharmacological properties. "Their anticholinergic action seems the most plausible since other drugs with central atropine-like action such as scopolamine hydrobromide and trihexyphenidyl (artane<sup>®</sup>) possess similar prophylactic properties." It does appear that marezine possesses a certain amount of protection against postoperative vomiting. No further episodes of vomiting occurred in 76.2 per cent of patients treated therapeutically with this drug. Cessation of this complication in the treated patients would be more significant if it were not for the fact that approximately 60 per cent of all patients have only one episode of vomiting without treatment. The prophylactic action of the drug, however, seems more evident. The incidence of vomiting in the group of 200 patients who did not receive the drug prophylactically was 18.5 per cent; in the group treated prophylactically the incidence was 10 per cent—a reduction of 45.8 per cent in favor of the treated group. It is interesting to note that in the group given general anesthesia and treated prophylactically, 4 of the 11 patients who did vomit had had cholecystectomies; this is an incidence of 36.4 per cent in this particular group of patients. We believe that the patients who had cholecystectomies would show a marked decrease in postoperative vomiting if, routinely, a Levin tube were put in place. This is not done in this institution. In the great majority of patients given general anesthetics the endotracheal method was used, and in agreement with Moore *et al.* (4) this may, to some extent, account for our seemingly lower incidence of postoperative vomiting. All patients were examined in the recovery room and on the wards for local redness and swelling. Aside from the one patient mentioned previously, there were no complications in the area of injection; in this patient injection may have been too superficial. With respect to the possibility of burning on injection, this might occur more frequently if the drug were administered to a completely conscious patient who had not previously been medicated or anesthetized. It is worth noting, however, that this complaint did not arise even in the patients who were given spinal anesthesia, and all injections were given in the deltoid area. There is probably an irreducible minimum with respect to postoperative vomiting, but from previous studies it would appear that an over-all incidence of vomiting of 10 per cent in all patients undergoing major surgical procedures approaches that minimum.

#### SUMMARY AND CONCLUSION

From this study of 322 patients who were treated for postoperative vomiting both prophylactically and therapeutically with marezine brand cyclizine hydrochloride<sup>®</sup>, the following conclusions are justified. (1) If marezine is employed in dosages of 50 mg. for adults and 25 mg. for children and is administered in the deep subcutaneous tissue one-half

hour before the contemplated end of the surgical procedure, the postoperative vomiting will be decreased. In this series it was reduced from 18.5 per cent to 10 per cent—a reduction of 45.8 per cent. (2) Marezine, administered therapeutically, seems to be of value in arresting further vomiting during the immediate postoperative period. This should be investigated more fully in an attempt to evaluate the usefulness of the drug if continued through the first twenty-four to thirty-six hours of the postoperative period. (3) In this series of 322 patients, the drug produced no local reaction and no untoward effects. (4) Further study and use of this drug for the purposes listed above are warranted by these results.

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