South African Medical Journal : Suid-Afrikaanse Tydskrif vir Geneeskunde

Cape Town, 25 March 1961 Volume 35 No. 12 Deel 35 Kaapstad, 25 Maart 1961

THE USE OF ANTI-EMETIC DRUGS IN ANAESTHESIA

M. H. HEYNS, M.B., CH.B. and C. S. JONES, M.B., CH.B.

Department of Anaesthesia, University of Cape Town, and Groote Schuur Hospital, Cape Town

From the point of view of the patient a distressingly common complication of anaesthesia, in particular of general anaesthesia, is nausea, retching and vomiting, and anaesthetists have long sought means of alleviating these unpleasant sequelae.

Advances in physiology and pharmacology have led to the postulation of the existence of emetic trigger zones and an emetic centre, either or both of which can be depressed by drugs and in particular by the group of phenothiazine derivatives. The anti-emetic properties of these drugs are bound up with other actions, some desirable and others less so. Thus, while the anaesthetist welcomes the drug which has a general tranquillizing effect in addition to an anti-emetic one, he may be embarrassed by an associated hypotensive action or by a prolongation of post-anaesthetic unconsciousness.

POST-ANAESTHETIC VOMITING

Some doubt has been thrown on the wisdom of trying to reduce the incidence of post-anaesthetic vomiting, particularly where these efforts may be associated with less desirable side-actions. Post-anaesthetic vomiting may be due to a number of factors, some of which, e.g. the vomiting due to bowel obstruction, are of diagnostic importance to the surgeon. In these patients drug-induced suppression of vomiting may prove a hazard in the post-operative period. There are, of course, non-surgical causes of post-anaesthetic vomiting such as hypoxia (compare this with the vomiting of mountain sickness) and the use of analgesics such as morphine and pethidine. But in these instances the use of drugs which, while suppressing vomiting, may increase hypoxia by producing hypotension, or by prolonging central-nervous-system depression with their potentiation of anaesthesia, is not lightly to be recommended.

Various studies of a variety of remedies for post-anaesthetic vomiting have been made from time to time and, not surprisingly, the results differ widely. The large number of causes and the tremendous individual variation in response to a single causative factor, make the interpretation of the results particularly difficult. As an illustration of this we wish to report the preliminary results of a 'double-blind' study of 3 different phenothiazine derivatives, each of which has been recommended as a valuable post-anaesthetic anti-emetic.

METHOD

Bellville *et al.*[1] have shown that women are about 3 times more likely than men to vomit in the immediate post-anaesthetic period. These authors have also suggested that the incidence of vomiting is higher following intra-abdominal operations or in patients more deeply anaesthetized for some other reason. The ability of the anaesthetist himself can also affect the incidence.

In order to make the test as searching as possible and at the same time to eliminate as many variables as possible, the patients for this study were drawn entirely from adult women who were scheduled for abdominal hysterectomy or oophorectomy. They were all premedicated, largely with morphine or pethidine and atropine or hyoscine (Table I). All the anaesthetics were administered by a single anaesthetist who used a standardized technique.

TABLE I. PREMEDICATION AND INCIDENCE OF VOMITING

Premedicating drugs and doses	*Number of patients*	*Number vomiting*	*Comments*
Morphine, 11 mg., and atropine, 0·65 mg.	7	3	Proportion vomiting is 20/48ths. There is no significant difference
Pethidine, 100 mg., and atropine, 0·65 mg.	29	11	Proportion vomiting is 18/48ths. There is no significant difference
Pethidine, 75 mg., and atropine, 0·65 mg.	3	1	Remaining groups are too small for statistical consideration. As a whole, proportion vomiting is 20/48ths, which is not significant
'Omnopon', 11 mg., and atropine, 0·65 mg.	2	1	
'Omnopon', 22 mg., and atropine, 0·65 mg.	1	—	
'Phenergan', 50 mg., and atropine, 0·65 mg.	1	—	
Not recorded	5	3	
Total	48	19	

Induction of anaesthesia was with small doses (100 - 300 mg.) of a 2·5% solution of intravenous thiopentone and nitrous oxide (6 l. per minute) and oxygen (3 l. per minute) by inhalation. The gases were administered *via* the Magill circuit of a Boyle's machine. Ether was added until the depth of anaesthesia was such that the technique could be safely changed. Thereafter anaesthesia was continued and maintained by the administration of ether dripped on the gauze of a Schimmelbusch mask. This open-drop administration was continued until the operation was almost completed and the anaesthetic could be stopped. Relaxation was secured by deepening the anaesthetic.

As soon as the administration of the anaesthetic had ceased, the anaesthetist administered, by intramuscular injection, the contents of an ampoule of the drug to be tested. At the end of the operation the patient was returned to the ward and observed for the next 12 hours by the nursing staff who looked, in particular, for vomiting. Vomiting was defined in advance as the production at the mouth of any fluid or solid material, other than sputum, in association with retching and straining.

The ampoules of drug for injection were prepared

TABLE II. DATA CONCERNING THE PATIENTS TESTED, AND RESULTS OF TRIAL

Drug	*Dose*	*Age in years (mean and range)*	*Height in inches (mean and range)*	*Weight in lb. (mean and range)*	*Duration of anaesthesia in minutes (mean and range)*	*Number in group*	*Number vomiting*	*Proportion vomiting*
Distilled water ..	2 ml.	43 (27 - 73)	64 (61 - 66)	152 (95 - 230)	63 (35 - 110)	12	6	24/48
Largactil	25 mg. in 2 ml.	42 (26 - 63)	65 (63 - 67)	142 (120 - 170)	54 (37 - 118)	12	4	16/48
Siquil	10 mg. in 2 ml.	37 (21 - 50)	63 (61 - 65)	129 (90 - 215)	63 (27 - 114)	12	3	12/48
Trilafon	5 mg. in 2 ml.	37 (28 - 46)	63 (60 - 64)	123 (110 - 150)	65 (30 - 113)	12	6	24/48
Whole group ..		39 (21 - 73)	64 (60 - 67)	137 (90 - 215)	61 (27 - 118)	48	19	19/48

in advance by someone else. In each instance the fixed dose of drug was made up to a volume of 2 ml. with sterile water and sealed in a sterile ampoule. The ampoules carried no identifying mark other than a number drawn at random from a pool of 360 numbers at the time of preparation. Only the person preparing the ampoules held the key relating the number of an ampoule to its contents. In order to provide an internal control, 1 batch of ampoules was filled with sterile distilled water only. The others contained either 25 mg. of chlorpromazine ('largactil'), 10 mg. of triflupromazine ('siquil'),* or 5 mg. of perphenazine ('trilafon').** There was an equal number of ampoules in each batch but they were all stored loosely in a single box before being handed over to the anaesthetist who was to use them. In this way neither the anaesthetist, nor the nurses observing the patients, were aware of what drug any particular patient had received.

RESULTS

Data concerning the patients who were the subjects of this study, and the results of the study, are set forth in Table II.

The application of the chi-square statistical test to the observed results in Table II, using the mean values as the expected values, shows that only triflupromazine (siquil) might possibly be of value as a post-anaesthetic anti-emetic drug in the doses used and under the circumstances of the study. To prove or disprove the value of this drug under similar circumstances this study must be extended to a further 100 subjects, half of them being controls.

* Made available by courtesy of Messrs. E. R. Squibb and Sons, P.O. Box. 38, Isando, Transvaal.

** Made available by courtesy of Messrs. Scherag (Pty.) Ltd., P.O. Box 7539, Johannesburg.

DISCUSSION

Particular note should be taken of the fact that the results here reported apply only to adult women undergoing abdominal hysterectomy or oophorectomy under the type of anaesthetic described above. Furthermore, the results must be studied in the light of the fact that an entirely arbitrary choice of drug dose was made. It is quite possible that with different doses, under altered circumstances, and with quite another anaesthetic technique, drugs here studied might show different results. But side-effects such as hypotension and prolonged waking time might prove troublesome in turn.

To perform controlled experiments covering the multitude of variables which can be deliberately altered and controlled in a study of this nature, would make a life-work for a team of several people. If consideration is also given to the large number of variables over which the experimenter has no control whatever (such as patient idiosyncrasy, blood loss, duration of operation) it is apparent that chance will play a very large part in determining the results of the clinical testing of new drugs under the circumstances which too often obtain in such clinical trials.

To the thoughtful practitioner, attempts to determine the cause of post-anaesthetic nausea and vomiting, and efforts to eliminate these causes, would appear to be a far more reasonable line of advance.

SUMMARY

A clinical trial of anti-emetic drugs is reported. The trial was rigidly controlled and results are largely equivocal.

The information of value arising from a trial of this nature is discussed.

We thank Dr. J. G. Burger, Medical Superintendent, Groote Schuur Hospital, for permission to publish details of these patients.

REFERENCES

1. Bellville, J. W., Bross, I. D. J. and Howland, M. D. (1960): Anesthesiology, **21**, 186.