REDUCTION OF POSTOPERATIVE VOMITING BY PREOPERATIVE ADMINISTRATION OF ORAL METOCLOPRAMIDE

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ABSTRACT

Preoperative oral metoclopramide was evaluated as a postoperative antiemetic agent.

Two series of approximately one hundred patients were investigated in this context. One series was carefully controlled with regard to anaesthetic agents and technique. The other series had only one criterion of admission – the exclusion of narcotics.

All patients received metoclopramide 20 mg by mouth or a placebo two hours before anaesthesia in a randomized double-blind fashion.

A significant reduction in postoperative symptoms of antiperistalsis was observed in the metoclopramide-treated patients.

On closer scrutiny it became apparent that, under these circumstances, metoclopramide is significantly more effective in males.

ALTHOUGH POSTOPERATIVE VOMITING is regarded as a minor complication of anaesthesia,¹ the incidence appears high enough to warrant investigation into the possibility of its reduction.²⁻⁷

Metoclopramide has been used before,^{3,6} during,^{8,9} and after surgery.^{4,5} The results of its administration on postoperative vomiting have been tested against placebo and the administration of other antiemetics^{7,9,10} and have favoured its use.

In all these series a parenteral route of administration has been adopted. We therefore undertook a study to evaluate the possible benefit of a preoperative oral dose of metoclopramide in reducing nausea, retching and vomiting in the postoperative period.

METHOD AND MATERIALS

Our patients were divided into two groups of approximately one hundred patients each and the two groups were investigated independently.

For Group I, 104 patients between the ages of 16 and 60 undergoing orthopaedic operations were chosen so as to eliminate intraperitoneal mechanical stimuli to vomit. Premedication consisted of lorazepam 0.04 mg · kg⁻¹ and, in a randomized double-blind fashion, either metoclopramide 20 mg or placebo.

This premedication was given orally two hours preoperatively. An identical dose of lorazepam was given the preceding evening as the night sedative.

Induction was by thiopentone and succinylcholine. The tracheae of all patients were intubated and artificial ventilation was employed with nitrous oxide-oxygen and either halothane or enflurane.

Since narcotics are included in many anaesthetic techniques, alphaprodine 0.2 mg · kg⁻¹ was given intravenously one half-hour before the anticipated termination of operation to present a central and peripheral pharmacological challenge that would also yield homogeneous results suitable for statistical analysis. These anaesthetics were all administered by one of us (M.J.D.).

Patients were monitored in the recovery room and on the ward by a trained observer. Any incident of nausea, retching or vomiting was counted as a failure and recorded as occurring in one of three time periods, that is 0–1, 1–3 and 3–6 hours postoperatively.

Group II. A further group of 102 patients was divided equally into orthopaedic procedures on the knee and abdominal hysterectomies. Inclusion in this group depended simply on the avoidance of narcotics for premedication and the anaesthetic. As in Group I, these patients were given metoclopramide 20 mg by mouth in a stratified (i.e. randomized within the two subgroups) double-blind fashion about two hours preoperatively.

While in the recovery room, patients in this group received hydromorphone administered in-

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TABLE I
INCIDENCE OF POSTOPERATIVE NAUSEA, RETCHING
AND VOMITING GROUP I

Postop time of incidence (hours)	Controls n = 49	Treatment n = 55	χ^2	p value
0-1	10	5	1.85	0.174 n.s.
1-3	11	3	5.04	<0.025
3-6	8	3	2.19	0.139 n.s.

TABLE II
INCIDENCE OF POSTOPERATIVE NAUSEA, RETCHING
AND VOMITING GROUP II

Time (hours)	Controls n = 53	Treatment n = 49	χ^2	p value
0-1	15	6	4.02	<0.05
1-3	24	9	8.42	<<0.01
3-6	7	5	0.22	n.s.

travenously and orally as soon as they complained of pain.

This group was monitored in the same way as Group I and any incident of nausea, retching or vomiting was recorded in the appropriate time period.

RESULTS

Following the collection of all data, the code was broken and the results analyzed by χ^2 test for both groups (Tables I and II).

Reduction in symptoms of postoperative antiperistalsis occurred during the time periods studied. This reached statistical significance during the 1-3-hour postoperative period in both groups.

We confirmed that our population of males and females was not significantly different in the orthopaedic patients of Group I or in the combined orthopaedic patients of Group I and Group II (Tables III and IV). We then examined the sex distribution of patients who vomited postoperatively and found that a highly significant difference existed between the males and females in the metoclopramide treated group (Table V). In fact the reduction in postoperative vomiting occurred much more in males, the statistical significance of which is extremely high ($\chi^2 = 16$ with Yates correction). In female patients undergoing hysterectomy we found a reduction in postoperative vomiting, but this trend did not reach statistical significance (Table VI).

TABLE III
GROUP I
SEX DISTRIBUTION OF 104 ORTHOPAEDIC PATIENTS

	Control	Treatment	χ^2
Male	29	31	N.S.
Female	20	24	N.S.

TABLE IV
GROUP I PLUS ORTHOPAEDIC PATIENTS IN GROUP II
SEX DISTRIBUTION OF 155 ORTHOPAEDIC PATIENTS

	Control	Treatment	χ^2
Male	45	46	N.S.
Female	31	33	N.S.
Total	76	79	N.S.

TABLE V
GROUP I PLUS ORTHOPAEDIC PATIENTS OF GROUP II
SEX DISTRIBUTION OF 47 (30% of 155) PATIENTS
VOMITING 0-6 HOURS POSTOPERATIVELY

	Control	Treatment	p
Male	19	2	<<0.001
Female	12	14	N.S.
Total	31	16	<0.01

TABLE VI
51 ABDOMINAL HYSTERECTOMIES

	Vomited	Did not vomit
Control	13	13
Treatment	17	8

The reduction in postoperative vomiting in the treatment group does not reach statistical significance.

DISCUSSION

The object of the study was to test the assumption that preoperative oral administration of metoclopramide is effective in reducing postoperative vomiting. A certain range of intervals between administration of the drug and the termination of operation is unavoidable and by the same token is desirable for this study to have practical application.

The exact mechanism of action of metoclopramide is not yet clearly understood. However, there is evidence of central and peripheral actions.

The central emetic action of narcotics may be overcome by metoclopramide.^{11,12} In parturient

females, McGary¹³ demonstrated both a decrease in stomach emptying time and a significant reduction of the emetic effect of meperidine using either metoclopramide or perphenazine. No difference between the drugs was noted in this context.

The peripheral action of metoclopramide is cholinergic. The tone of the lower oesophageal sphincter is reduced by atropine¹⁴ and increased by metoclopramide.¹⁵

Stomach emptying time is reduced as evidenced by the more rapid appearance of diazepam¹⁶ and acetaminophen^{17,18} in the bloodstream.

Both central and peripheral actions foster physiological peristalsis and counteract the antiperistaltic action of narcotics, anticholinergics and pregnancy.

A favourite experimental model in antiemetic studies is the patient undergoing dilatation and curettage. A large number of short procedures not involving peritoneum may be accumulated under controlled conditions and evaluated in a relatively short time.

Thus the successful demonstration of metoclopramide as an antiemetic has involved predominantly female patients. Our data suggest a more potent action in males. This greater efficacy seen in males in this dose range may be due to pharmacokinetic differences between males and females resulting in greater clearance or larger volume of distribution or, less likely, a gender-dependent pharmacodynamic difference. No explanation for this observation is possible at this time.

Nevertheless, a drug which promotes peristalsis, counteracts antiperistalsis and reduces postoperative vomiting is surely valuable to the anaesthetist.

Our practice of oral premedication has the obvious advantage of being more pleasant than the parenteral route while being just as effective and costing only about one-third.

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RÉSUMÉ

Les auteurs évaluent à la période post-opératoire l'activité anti-émétique de la métoclopramide administrée par la voie orale avant l'intervention.

Deux groupes de cent malades environ ont été étudiés dans ce but. L'homogénéité d'un des groupes fut contrôlée avec soin en ce qui concern l'agent et la technique anesthésiques. L'autre groupe n'avait qu'un critère d'admission, soit l'absence de narcotique.

Tous les patients reçurent métoclopramide 20 mg per os ou un placebo deux heures avant l'anesthésie selon une méthode randomisée à double inconnue.

Une diminution significative des symptômes d'antiperistalsisme a été observée chez les patients traités à la métoclopramide et plus spécialement chez ceux du sexe masculin.