DOUBLE-BLIND EVALUATION OF METOCLOPRAMIDE (MK 745, SINEMET®), TRIMETHOBENZAMIDE (TIGAN®), AND A PLACEBO AS POSTANAESTHETIC ANTI-EMETICS FOLLOWING METHOXYFLURANE ANAESTHESIA*

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ONE OF THE COMMONEST COMPLICATIONS of anaesthesia and surgery is the occurrence of nausea, retching, and vomiting. The action of anaesthetic and associated drugs directly upon the digestive tract and its central and peripheral innervation probably play a prominent role on its incidence (see Table I).^{1,2} Many non-specific prophylactic and therapeutic measures have been employed to prevent or reduce its occurrence with but variable success (see Table II).^{3,4}

Numerous drugs have been shown to have a depressant effect on the vomiting induced by chemical agents in dogs and other animals.² Unfortunately, it is not as easy to reproduce the usual clinical factors which appear to initiate vomiting in man, so that it is practically useless to attempt to prove the efficacy of an anti-emetic drug by animal experiments alone.⁵⁻⁷

Several other factors must be considered before it is decided to use an anti-emetic agent in man in order to be sure that it is indeed useful following anaesthesia. First, the anti-emetic drug should be free of an appreciable depressant effect on the circulation and on respiration in the dose which might suppress postanaesthetic vomiting. The agent should be non-toxic to vital organs, and it should not prolong the hypnotic effect of anaesthetics or itself cause marked drowsiness. Very few of the drugs currently available as anti-emetics have such a limited action. Furthermore, the brief duration of the anti-emetic effect of these drugs substantially limits the optimum time for their administration.⁸⁻¹⁵

Metoclopramide (MK 745) was developed in France in 1963, where it is known as Primpéran. Its anti-emetic action was said to be powerful whether vomiting is of central or peripheral origin in a variety of clinical conditions in man. The formula is shown in Figure 1.

Metoclopramide hydrochloride

4-amino-5-chloro-N-[2-(diethylamino)ethyl]
-o-anisamide hydrochloride

$C_{14}H_{22}ClN_3O_2 \cdot HCl$

FIGURE 1. Structural formula of metoclopramide.

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TABLE I
ACTION OF ANAESTHETIC AND ASSOCIATED DRUGS UPON THE DIGESTIVE TRACT

site	Action		Effects		Examples			
	mode	muscle	sphincter	secretions	premedication	anaesthetic drugs	associated drugs	anoxia
Sympathetic postganglionic	{ adrenergic anti-adrenergic	relaxation increased tone	relaxation ?spasm	decrease ?nil	?antihistamines	?light ether ?fluothane, penthrane	vasopressors	early stages
Parasympathetic	{ cholinergic or anticholinesterase anticholinergic	increased tone relaxation from above down	increased tone relaxation	increase decrease from above down	morphine atropine demerol	spinal pentothal cyclopropane	prosthigmine mytolon	
Ganglia	{ sympatholytic antiadrenergic parasympatholytic anticholinergic	increased tone decreased tone		vary vary	phenothiazines phenothiazines			
Peripheral nerves		nil to possible inhibition						
Direct	{ tonic depressant	increased tone relaxation	spasm relaxation			irritant agents causing reflexes all potent agents (degree $\propto$ depth)	pitressin procaine	
Blood vessels	{ hypotensive hypertensive	decreased tone Varies with degree of vasodilatation or vasoconstriction	relaxation	$\propto$ blood flow	demerol papaverine phenothiazines droperidol	deep anaesthesia	C ₆ Arfonad, Veratrum, etc.	late stages early stages
Smooth muscle	histamine release	increased tone		increased	?morphine		curare (occasionally)	
Nervous system	depressant				morphine demerol	depression of reflexes $\propto$ depth		all stages

TABLE II
GASTROINTESTINAL COMPLICATIONS RELATED TO ANAESTHESIA

Complications	Prophylactic and therapeutic measures
<p>I. Nausea and vomiting Incidence: 1936—ether 56.5%, cyclopropane 39%, N₂O 23%, ethylene 33%; 1967—should not exceed 20%: halothane, methoxyflurane</p> <p>Causation</p> <ol style="list-style-type: none"> specific reflex vomiting possible allergy reflex stimuli; commonest related causes: <ol style="list-style-type: none"> ill-prepared patient (psychically disturbed, full stomach, depressed metabolic function—starvation, dehydration, electrolyte imbalance, ketosis) inadequate or ill-timed premedication incorrect technique of induction: gastric irritation—reflex vomiting, anoxia, other insulting reflexes direct effect of drugs which produce ketosis (depth and duration, type of agent, inadequate replacement of fluids, inadequate oxygenation) stormy emergence underlying pathology; frequent unrelated causes: <ol style="list-style-type: none"> intestinal obstruction peritonitis biliary and renal colic tabetic crises pancreatitis cerebral diseases uraemia (incipient) pregnancy (abnormal) 	<ol style="list-style-type: none"> proper preparation for elective surgery; careful examination of emergency cases individual properly timed premedication rapid, smooth induction with full oxygenation; light anaesthesia; avoid toxic drugs obtain relaxation with peripheral blocking agents; use specific fluids and electrolytes during operation proper postoperative care and observation
II. Persistent vomiting (gross water and salt imbalance)	Early attention to details
III. Silent vomiting (atony of tract and sphincters)	Effective gastric suction
IV. Aspiration of vomitus	Awareness of possibility; wash out stomach; gastric suction; cuffed endotracheal tube
V. Distension	Avoid deep, long anaesthesia; postoperative suction, cholinergic drugs, oxygen therapy
VI. Aggravation of paralytic ileus	
VII. Rupture of obstructed gut following spinal	Selection of anaesthetic varies with degree of distension

The acute and chronic toxicity of this compound has been shown to be extremely low. Initial trials in animals have indicated that it has a wide margin of safety, is well tolerated and does not affect the blood, liver, kidneys, or autonomic nervous system, and has no teratogenic effects. When used in association with anaesthesia, no respiratory or cardiovascular disturbances have been observed. It has been shown to be far more potent than chlorpromazine, diphenhydramine, prochlorperazine, and trimethobenzamide against apomorphine, Hydergine®, and copper sulphate induced vomiting in animals. It has no anti-acetylcholine, anti-histaminic, or anti-serotonin effect; it is ten times *less* likely to produce extrapyramidal disturbances than thiethylperazine and chlorpromazine, and it is 30 times *less* sedative than chlorpromazine. The only commonly

encountered side-effect in man was mild drowsiness when it was taken orally. Agitation has occurred in some elderly patients receiving the drug at a high dose level, and they felt better when the dose was reduced.^{16,17}

This report deals with a double-blind comparison of metoclopramide with trimethobenzamide (Tigan®) and an inert placebo, to determine whether the active drugs reduce post-anaesthetic nausea and vomiting. Trimethobenzamide was chosen as the comparative agent because it is also relatively free from undesirable side-effects, and some reports have indicated that it might be an effective anti-emetic following general anaesthesia if given in a dose higher than that recommended by the manufacturer (300 mg. instead of 200 mg.).¹⁸⁻²¹

METHOD

The effectiveness of a single injection of metoclopramide (20 mg.), trimethobenzamide (300 mg.), and a placebo (lactose) was studied by the double-blind method in 284 adult patients, all of whom were elective cases scheduled for major upper abdominal operations. In each patient, anaesthesia was induced with gallamine 80 to 120 mg. and thiopental 200 to 400 mg. Then, following oxygenation and orotracheal intubation, anaesthesia was maintained with less than 1.5 per cent methoxyflurane delivered from a Pentec vaporizer (placed outside the circuit of the gas machine) plus 60:40 nitrous oxide:oxygen administered in a semi-closed system. Pulmonary ventilation was controlled adequately with a respirator until the abdominal fascia was closed. The anaesthetic agents were then discontinued and breathing was controlled or assisted with oxygen alone until adequate spontaneous respiration resumed. A nasogastric tube was in place or inserted during the operation, and suction was attached post-operatively in approximately two-thirds of the patients only at the surgeon's request.

Approximately 30 minutes before the end of each operation, one of the preparations under study was administered intravenously. The order of assignment of the drugs followed a random number code. The identity of the substance was not known to the anaesthetist, who merely recorded the code number of the drug on his anaesthetic record after he administered the material. After the test drug was administered, vital signs, clinical signs, and symptoms related to the study were observed closely for the first six hours by a nurse who was trained for this work. The patient's chart was reviewed 24 hours postoperatively to record the incidence of nausea and vomiting and related information. The identity of the compounds administered was not revealed to the principals involved in the study until the study was completed and all the data were tabulated.

Upon completion of the study, all pertinent data were punched on IBM cards for subsequent detailed analysis.

RESULTS

The patients who developed nausea and/or vomiting are listed in Tables III, IV, and V, which show the age (A); sex (S); ponderal index (PI); premedication

TABLE III
INCIDENCE OF NAUSEA AND VOMITING AMONG THE PATIENTS WHO RECEIVED THE PLACEBO
(47 F + 47 M = 94 Pts.)

	Test no.	A	S	PI	Premed.	Operation	NGT	Anaes. time	Delay in wakeup	N	V	Narcotic within 4 hrs.
1	4	29	F	11.29	AM	3	0	320	0	0	12.00	0
2	9	52	M	11.19	AM	3	0	325	225	0	*3.50	0
3	15	65	M	12.41	AM	3	1	245	0	.45	0	0
4	22	27	F	11.90	A	1	0	130	110	6.00	*1.20	0
5	26	35	F	10.12	AM	1	0	200	45	3.00	*24.00	+
6	29	43	F	9.28	AM	3	0	220	0	0	6.00	0
7	49	78	F	—	A	3	1	210	50	1.20	0	0
8	60	71	F	—	AM	2	1	320	0	3.00	0	0
9	77	50	F	10.83	AM	2	0	350	50	3.50	0	+
10	79	46	M	9.65	AM	3	1	435	20	4.50	0	+
11	84	49	M	12.33	AM	3	0	430	20	10.00	0	0
12	98	44	F	11.00	AM	1	0	130	5	6.30	*6.30	0
13	121	32	F	11.96	AM	3	0	230	45	8.00	8.00	+
14	124	61	F	12.44	AM	3	1	330	15	5.30	*8.00	+
15	149	72	F	12.19	A	1	0	110	100	0	8.45	0
16	184	53	F	12.67	A	2	1	330	100	0	7.00	0
17	197	34	F	11.84	A	1	1	315	100	1.00	1.00	0
18	203	19	F	12.00	A	1	0	150	30	1.00	1.00	+
19	207	40	F	11.12	A	1	0	115	45	0	*12.00	0
20	213	32	F	11.78	A	1	0	135	0	0	5.30	0
21	248	36	F	11.63	A	1	1	240	30	12.00	0	+
22	253	40	F	11.55	A	1	1	135	110	24.00	0	+
23	266	26	F	12.37	A	1	1	145	35	0	14.00	0
24	278	40	F	10.31	AM	3	1	335	10	5.00	0	0
25	291	55	F	—	A	1	1	135	35	4.00	0	+

*Recurrent (6).

TABLE IV
INCIDENCE OF NAUSEA AND VOMITING AMONG THE PATIENTS WHO RECEIVED METOCLOPRAMIDE
(60 F + 36 M = 96 Pts.)

	Test no.	A	S	PI	Premed.	Operation	NGT	Anaes. time	Delay in wakeup	N	V	Narcotic within 4 hrs.
1												
2	2	47	F	10.49	AM	1	0	240	0	0	4.00	0
3	11	69	F	11.19	AM	3	0	120	0	0	*2.15	+
4	25	55	F	13.54	AM	3	0	120	15	6.00	*9.00	+
5	50	37	F	—	AM	1	0	185	60	1.00	0	0
6	65	66	M	12.75	AM	3	0	750	0	0	5.00	0
7	68	62	M	12.59	AM	2	1	445	45	0	*7.00	0
8	71	63	F	12.59	AM	2	0	150	30	5.00	0	0
9	73	72	F	—	AM	3	0	345	115	6.00	*6.00	+
10	82	48	M	10.87	AM	3	0	200	0	5.00	5.00	+
11	85	29	F	11.34	AM	3	0	300	35	6.00	*9.00	0
12	92	59	M	10.43	AM	1	1	155	30	3.00	0	0
13	99	63	M	10.70	AM	3	0	140	30	6.40	0	0
14	101	36	F	12.26	AM	3	1	415	25	5.00	7.00	+
15	112	40	F	12.23	AM	2	1	530	15	0	1.15	0
16	139	66	F	10.70	AM	3	1	330	100	4.00	*4.00	+
17	171	48	F	11.12	A	3	1	330	100	1.00	1.00	+
18	254	48	M	12.63	A	1	0	235	100	0	*14.00	+
19	267	30	F	10.29	A	1	0	300	30	0	30	0
20	270	67	F	9.93	A	1	0	145	0	6.00	0	0
21	290	44	F	11.84	A	1	0	115	30	7.00	7.00	0
22	292	60	F	—	A	3	0	200	100	24.00	0	0
										1.30	0	0

*Recurrent (7).

TABLE V
INCIDENCE OF NAUSEA AND VOMITING AMONG THE PATIENTS WHO RECEIVED TRIMETHOENZAMIDE
(52 F + 42 M = 94 Pts.)

Test no.	A	S	PI	Premed.	Operation	NGT	Anaes. time	Delay in wakeup	N	V	Narcotic within 4 hrs.
1	10	64	M	AM	3	1	320	50	0	15.00	0
2	14	43	F	AM	3	1	315	55	13.00	0	+
3	28	60	F	AM	3	0	300	100	2.50	*12.00	0
4	33	54	F	AM	2	1	210	245	12.00	0	0
5	45	53	F	AM	1	1	150	45	12.00	*13.00	0
6	46	49	F	AM	3	0	240	0	12.00	*12.00	0
7	53	61	F	AM	3	0	195	0	0	*3.00	0
8	64	49	F	AM	3	0	230	0	4.00	0	0
9	80	31	F	AM	1	1	300	45	2.00	24.00	0
10	83	75	F	A	3	1	200	40	1.00	6.00	0
11	88	29	F	A	3	0	145	30	0	4.00	0
12	97	36	M	AM	1	0	150	55	0	*2.50	0
13	140	22	F	A	3	0	230	0	4.15	24.00	+
14	160	62	F	A	1	1	445	100	2.15	2.15	+
15	164	57	M	AM	2	1	150	45	1.45	0	+
16	168	66	F	AM	1	1	300	30	6.00	0	+
17	190	29	M	A	1	1	215	20	1.00	0	+
18	217	44	F	A	1	0	215	20	14.00	0	+
19	227	28	M	A	1	1	215	0	24.00	*9.45	+
20	238	45	F	A	1	0	60	20	9.00	9.00	0
21	242	38	F	AM	1	1	205	5	0	24.00	0
22	244	51	F	AM	1	0	210	50	0	12.00	0
23	255	51	F	A	1	0	135	35	12.00	12.00	0
24	293	76	F	AM	2	0	155	45	24.00	16.00	0

*Recurrent (6).

used (A = atropine, M = meperidine); operation (1 = cholecystectomy, 2 = gastrectomy, 3 = other major abdominal surgery); whether a nasogastric tube was inserted prior to or during the operation; anaesthesia time in minutes; delay in postanaesthetic awakening in minutes; the hour after awakening when nausea or vomiting first occurred, and whether a narcotic was administered for the relief of pain within four hours prior to the occurrence of nausea or vomiting.

Placebo Group (See Tables III, VI, and VII)

Twenty-five out of 94 patients experienced nausea and/or vomiting. In 13 patients, symptoms were present in the first six hours, and recurrent vomiting was present in six patients. The occurrence of nausea and vomiting was substantially greater among the females than the males (5:1). In approximately one-third of the patients, symptoms occurred within four hours after a narcotic was given for pain relief (9 of 25 patients). The use of a nasogastric tube appeared to reduce the incidence considerably (50%). During the recovery period there was no appreciable change in the blood pressure which could be attributed to the administration of the placebo.

Metoclopramide Group (See Tables IV, VI, and VII)

Twenty-two out of 96 patients experienced nausea and/or vomiting. In 13 patients, symptoms were present in the first six hours and recurrent vomiting was present in seven patients. The occurrence of vomiting appeared approximately

TABLE VI
EFFECT OF USING NASOGASTRIC SUCTION ON THE INCIDENCE OF NAUSEA AND VOMITING

	Nasogastric suction used	No. of patients	Nausea only	Nausea and vomiting	Per cent nausea and vomiting
Placebo	No	33	2	11	40
	Yes	61	8	4	20
Metoclopramide	No	39	7	10	44
	Yes	57	2	5	12
Trimethobenzamide	No	31	3	9	39
	Yes	63	6	7	21

TABLE VII
EFFECT OF ANTI-EMETIC TEST DRUGS ON SYSTOLIC BLOOD PRESSURE

	Placebo group		Metoclopramide group		Trimethobenzamide group	
	females (47): SBP±SEM	males (47): SBP±SEM	females (60): SBP±SEM	males (36): SBP±SEM	females (52): SBP±SEM	males (42): SBP±SEM
Induction	129±4	135±3	129±3	131±4	140±4	131±3
20 min. anaesthesia	114±3	118±3	118±2	117±4	125±3	116±3
End of anaesthesia	130±4	134±3	128±2	129±3	138±3	128±3
Postoperative (30 min.)	133±4	139±4	136±3	162±24	159±17	153±21

SBP = Systolic blood pressure.
SEM = Standard error of mean.

twice as often in the females. Narcotic medication was associated with symptoms in eight of the 22 patients. Symptoms occurred in 44 per cent of the patients who did *not* have nasogastric suction, whereas only 12 per cent had symptoms among those who did have nasogastric suction. There appeared to be a moderate *elevation* of the blood pressure in the male patients in the immediate post-anaesthetic period that might be attributed to the metoclopramide. There was no apparent increase in the incidence of slow recovery from anaesthesia in this group compared to the placebo group.

Trimethobenzamide Group (See Tables V, VI, and VII)

Twenty-four out of 94 patients had nausea and/or vomiting. In 13 patients, symptoms were present in the first six hours and recurrent vomiting was present in six patients. The incidence of vomiting was three times greater in females. Narcotic medication was associated with symptoms in six of the 24 patients. As in the other two groups, symptoms were present twice as often in the patients who did *not* have nasogastric suction postoperatively—39 per cent versus 21 per cent in the patients with nasogastric suction. The incidence of slow awakening after the anaesthetic in this group was similar to that seen in the other two groups. Moderate blood pressure elevation was evident in the males in this group, as occurred in the metoclopramide group.

DISCUSSION

The anaesthesiologist has become much more skeptical toward the prophylactic use of anti-emetic drugs because there are numerous factors which augment or override the effects of these drugs after an operation under general anaesthesia, so that it is often difficult to identify a clear-cut action.^{12,15}

It is well established that females vomit after anaesthesia and surgery more often than males, even after the same type of anaesthetic management and after the same surgical procedures.^{18,19} This observation was also made in this study. There could not be psychic interference on the part of the patient as far as this observation was concerned since none of the patients was awake when the test drugs were given.¹²

For major abdominal surgery, it appears important to institute nasogastric suction to remove fluids from the upper gastrointestinal tract. Although this measure is not always employed by the surgeon, it appears to be the most useful single measure for reducing the incidence of nausea, retching, and vomiting in the first 24 hours after major abdominal surgery. In this study, this single measure appeared to reduce the incidence of vomiting by 50 per cent.

This study confirmed our previous observation that, when methoxyflurane is used as the primary anaesthetic for major abdominal surgery, in the absence of preventive measures (no nasogastric suction and administration of narcotics for premedication), there is a 40 per cent incidence of nausea, retching, and vomiting.²²

We also observed that, in approximately 30 per cent of patients who had these gastrointestinal discomforts, they were closely related to the prior administration of narcotic analgesics for the relief of pain. This observation is worth further

study, since there are now available analgesic compounds such as methotrimeprazine which has a potent anti-emetic effect as well as a useful analgesic property.

This study confirmed previous observations which showed that trimethobenzamide does not appreciably affect the blood pressure or prolong anaesthesia even when given intravenously in relatively high dosage, but it also had no appreciable prophylactic effect on the incidence of postanaesthetic vomiting even when 50 per cent more than the recommended dose was administered.¹⁸⁻²¹

Metoclopramide did not have any significant effect on the blood pressure nor did it prolong anaesthesia, but it also appeared to be ineffective in reducing postanaesthetic gastrointestinal disturbances. Upon a detailed review of our data, the only difference observed in this group, when compared to the patients who received a placebo or trimethobenzamide, was a slightly lower incidence of nausea and vomiting among the patients who had nasogastric suction.

On the basis of this report and numerous previous observations, it appears useless to attempt to reduce the incidence of postanaesthetic nausea and vomiting by the prophylactic administration of anti-emetic drugs either as premedication or just prior to the termination of an anaesthetic.²³ The only measures which might be more effective, aside from selecting anaesthetic agents which inherently have minimal emetic properties, are the measures which ensure the mechanical removal of fluids from the upper gastrointestinal tract for up to 24 hours after a major abdominal operation and the use of the minimum effective dose of narcotic analgesic drugs when they are required for relief of pain. The only anti-emetic drugs which might further reduce the incidence of nausea and vomiting postoperatively should be expected by their nature to prolong the period of anaesthetic "sleep"; they almost invariably tend to reduce the blood pressure. Perhaps this is the price that will have to be paid until better therapeutic measures are discovered.

SUMMARY AND CONCLUSIONS

A double-blind comparison of a placebo, metoclopramide, and trimethobenzamide was carried out on 284 adult patients who were scheduled for elective major upper abdominal surgery under methoxyflurane-nitrous-oxide anaesthesia. The drugs were given intravenously, according to a random assignment number code, approximately 30 minutes before the end of an operation. Vital signs and other signs and symptoms were observed by a trained nurse and were recorded for six hours after the test drug was administered. Each patient's record was reviewed 24 hours after the operation to obtain follow-up data.

Metoclopramide (20 mg.) and trimethobenzamide (300 mg.) were not better than the placebo with respect to the incidence of nausea and vomiting during the first twenty-four hours after an operation in the patients that did *not* have nasogastric suction. The patients who had nasogastric suction postoperatively had at least 50 per cent lower incidence of nausea and vomiting. This effect was particularly prominent in the patients who received metoclopramide.

In approximately one-third of the patients who developed nausea and vomiting, these symptoms were associated with the prior administration of a narcotic

analgesic within four hours whether or not they received a potentially active anti-emetic drug.

Neither metoclopramide nor trimethobenzamide appeared to have any undesirable effect on the respiration, circulation, or rate of recovery from methoxyflurane anaesthesia.

On the basis of this study, it appears that neither of the anti-emetic compounds is effective in reducing the incidence of nausea and vomiting associated with the administration of methoxyflurane-nitrous-oxide anaesthesia for major upper abdominal operations. The administration of narcotic analgesic drugs appeared to be an initiating factor in about one-third of the patients who developed nausea and vomiting postoperatively. The only treatment which appeared to reduce the incidence of this complication effectively was the application of nasogastric suction.

RÉSUMÉ

On a fait une étude comparée d'un placebo, de la métoclopramide et de la triméthobenzamide chez 284 adultes qui devaient subir une intervention élective majeure dans la moitié supérieure de l'abdomen sous anesthésie au méthoxyflurane-protoxyde-d'azote. Les produits, désignés seulement par un numéro, étaient donnés par voie veineuse environ 30 minutes avant la fin de l'opération. Durant les six heures qui suivaient l'administration du produit, une infirmière compétente enregistrait les signes vitaux et les autres signes ou symptômes qui se produisaient. On revisait le dossier de chaque malade 24 heures après l'opération pour recueillir les données observées.

La métoclopramide (20 mg.) et la triméthobenzamide (300 mg.) n'étaient pas supérieures au placebo en regard de la fréquence des nausées et des vomissements durant les premières 24 heures qui suivaient l'opération, chez les malades qui n'étaient pas soumis à l'aspiration naso-gastrique. Les malades soumis à l'aspiration voyaient diminuer d'au moins 50 pour cent les nausées et les vomissements. Ceci était surtout évident chez ceux qui avaient reçu de la métoclopramide.

Chez environ un tiers de ceux qui ont eu des nausées et des vomissements, ces symptômes étaient associés à l'administration préalable d'un analgésique narcotique moins de quatre heures auparavant, qu'on ait donné ou non une médication antimétique active.

Ni la métoclopramide ni la triméthobenzamide n'ont semblé avoir d'effets secondaires sur la respiration, la circulation ou la durée du réveil de l'anesthésie au méthoxyflurane.

D'après cette étude, il s'avère que ni l'un ni l'autre des produits antiémétiques n'est efficace pour diminuer la fréquence des nausées et des vomissements après l'anesthésie au méthoxyflurane-protoxyde-d'azote pour les opérations à la partie haute de l'abdomen. L'administration de produits analgésiques narcotiques a semblé un facteur déclenchant chez environ un tiers des malades qui ont souffert de nausées et de vomissements post-opératoires. Le seul traitement qui a semblé efficace pour diminuer la fréquence de cette complication a été l'aspiration nasogastrique.

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