

(i)

DECLARATION

CANDIDATE

This dissertation is my own original work and has not been presented for a degree in any other University.

Signed:_____

SUPERVISOR

This dissertation has been submitted for examination with my approval as University Supervisor.

Signed:_____.

(ii)
TITLE

POST OPERATIVE VOMITING INCIDENCE
IN PATIENTS FOLLOWING MINOR
GYNAECOLOGICAL OPERATIONS USING
THREE VOLATILE ANAESTHETICS AND
ANTI-EMETIC EFFECTIVENESS OF
RODAVAN AND METOCLOPRAMIDE

BY

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SUMMARY

Post-operative vomiting incidence and anti-emetic effectiveness of Rodavan (chlorphenoxamine hydrochloride 30 mg., 8 chlorotheophylline 20 mg., and caffeine 50 mg.) and metoclopramide (plasil) were studied in four hundred and twenty (420) healthy Kenyan females undergoing either dilatation and curettage or evacuation of the uterus following incomplete abortion. These were divided into two groups:- A and B.

A

Consisted of three hundred (300) patients out of the total four hundred and twenty. These were neither pre-treated pre-operatively with pethidine nor anti-emetics (Rodavan or metoclopramide). They were further divided into three (3) sub-groups of a hundred patients each; for studying the incidence of vomiting following anaesthesia with diethyl-ether, halothane and trichloroethylene respectively. Each of the agent was administered in nitrous oxide and oxygen (2:1) via a mask and semi-closed Magill circuit (Mapleson A). Halothane concentration inspired was up to 1%. Each patient received also ergometrine 0.5 mg. during or immediately at the end of the operation. Patients were nursed in theatre suite recovery ward until awake before being transferred to the gynaecological emergency ward. The observation for vomiting or retching in the recovery ward was carried out

by a nurse under close instruction and supervision of the author during the first one hour post-operatively and subsequently for another five hours on the ward by ward nurses with the aid of special instructions. The incidence of nausea was not investigated as nausea was regarded as subjective and would have involved interrogation. Vomiting in all groups was noticed to occur during the first post-operative hour and that due to diethyl-ether (in 501) tended to occur during surgery. No attempt was made to grade the severity of vomiting or retching. The latter was regarded as vomiting. The incidence of vomiting during the immediate post-operative six hour period for diethyl-ether, halothane and trichloroethylene was 11%, 101 and 91 respectively. These figures gave an overall post-operative vomiting incidence of 12% in the three hundred patients. The differences in the vomiting incidence between these three agents were not statistically

2

significant (diethyl-ether and halothane, $X = 2.1$ $P > 0.1$, diethyl ether and trichloroethylene $X^2 = 2.82$ $P > 0.05$). The incidence of post-operative vomiting in healthy African females following dilatation and curettage or evacuation of the uterus after incomplete abortion would appear low when compared to figures obtained in Caucasians.

B

As diethyl-ether produced the highest incidence of post-operative vomiting amongst the three agents, and

as it is also the most commonly used inhalational anaesthetic in Kenya and Uganda, it was therefore chosen for studying the influence of pre-treatment with pethidine, Rodavan or metoclopramide on the incidence of post-operative vomiting following anaesthesia (with diethyl-ether).

The post-operative incidence of vomiting in twenty(20) patients who received pethidine 50 mg. each intravenously immediately before anaesthesia with diethyl-ether was 5% (1 case). The number of patients investigated was perhaps too small to enable a reliable comparison. Statistically, there was no significant difference.

Following pre-treatment with either metoclopramide 10 mg. intravenously immediately before or Rodavan 2 tablets orally two hours before induction of anaesthesia, the incidence of post-operative vomiting after diethyl-ether anaesthesia was 10% for either drug. In either case the reduction in incidence of vomiting from 17% to 10% was not statistically significant ($X^2=2.09$, $P> 0.1$). It was noted that, unlike with metoclopramide, Rodavan did not cause hypotension or dizziness. Rodavan is however slightly more expensive than metoclopramide and it is available only as tablet or suppository. For the ease of administration and freedom from undesirable side effects mentioned above, Rodavan would appear preferable to

metoclopramide in conditions where there is shortage of skilled nursing staff. Metoclopramide, because it can be given parentally, would appear useful in both prevention and treatment of post-operative vomiting.

1. INTRODUCTION

Post-operative nausea and vomiting has been a problem in anaesthesia for many years. It is distressing to the patient and makes fluid and electrolyte management difficult especially in children (1). Children in most cases are dehydrated pre-operatively and because of their size, have small reserves. Holden et al (2) in their study on children undergoing adenotonsillectomy, observed that about 62% of the patients had less than half the calculated pre-operative fluid requirement needed to maintain normal fluid balance (2).

Post-operative vomiting may result into complications which may influence a patient's prognosis adversely. For example Mendelson's syndrome (aspiration syndrome) (3,4), Mallory Weiss Syndrome (oesophageal mucosa tears) and Boerhaave syndrome (oesophageal rupture) (5,6). However, Mallory Weiss Syndrome and Boerhaave syndrome are rarely seen nowadays as complications of post-operative vomiting due to improved anaesthetic techniques used. Mendelson's Syndrome, which was first described in 1946 (3), is still a common complication and carries a high mortality especially in obstetric anaesthesia. Most of the obstetric patients present as emergency cases and are therefore not prepared for anaesthesia. Many workers have written extensively on Mendelson's syndrome and have recommended various ways

of preventing it. Such as starvation of patients for at least six hours before operation where possible, emptying of the stomach with either a wide-bore tube or emetics, and a two hourly administration of magnesium trisilicate. Many of these methods are still controversial and may not guarantee safety: the hall mark of prevention of Mendelson's syndrome is the cricoid pressure (7). Retching and coughing increase venous pressure which may cause reactionary bleeding endangering the viability of the skin graft or flap in plastic surgery (8). They also cause increase in intracranial pressure in neurosurgical patients and can result in significant loss of vitreous humour in patients with penetrating injuries of the eyes.

Several drugs have been used over the years in management of post-operative vomiting. The most popular ones have been metoclopramide (9-15), butyrophenones (16-19), phenothiazines (20,21,13,12,1,19) and domperidone (22,23).

The objectives of this study were:-

& JSS&VPJav f2?<? J^rJJ/m^ <?f W J S - ^ / ' J S J A ?
females undergoing evacuation of the uterus after incomplete abortion and dilatation and curettage when using diethyl-ether, halothane and trichloroethylene; and to compare the anti-emetic effectiveness of two drugs; Rodavan(Chlorpheno-

xamine hydrochloride 30 mg., 8 chlorotheophylline 20 mg and caffeine 50 mg.) and metoclopramide (plasil), and to find out which one was superior to the other. Therefore the study sets out to test the following hypothesis

- (a) "Post-operative vomiting is common in African females undergoing minor gynaecological operations.
- (b) Rodavan is as effective an anti-emetic as metoclopramide in reducing post.-operative incidence of vomiting'

2. MATERIALS AND METHODS

2.1 SELECTION OF PATIENTS

A total of four hundred and twenty healthy (A.S.A. I or II) (24) female patients were studied. All were undergoing either evacuation of the uterus or dilatation and curettage at the Kenyatta National Hospital. Their ages ranged from 15 - 49 years and weights from 40 - 80 kg. They were selected from gynaecological emergency lists over a period of six months, during which a total of one thousand three hundred and five females underwent similar procedures. Using part one of the proforma (fig. I) history taking and physical examination were carried out in each case before premedication. Anyone found with pallor, fever, a systolic blood pressure of less than 90 mmHg and any systemic disease, was excluded from the study. It is well known that some of these factors either alone or combined can cause nausea and vomiting (24,25). Any patient in good physical status and on the emergency list was selected for the study.

Following the sequence in which they came to the hospital, selected patients were divided into three groups; that is incidence or group I, the pethidine/group II, and the anti-emetic/group III. The incidence group consisted of the first three hundred patients on the list while the pethidine group consisted of the next twenty patients and antiemetic group, the last hundred patients respectively. All were starved for a minimum period of six hours as a

preventive measure against dangers associated with a full stomach (3).

2.2 ANAESTHETIC TECHNIQUE

All patients received atropine in doses of 0.6 mg. intramuscularly half an hour before induction of anaesthesia. In addition, fifty patients in group three, received 2 tablets of the anti-emetic Rodavan orally 2 hours before anaesthesia. Both drugs were administered and recorded in the proforma by the nurse on the ward. The patients were then transferred to theatre whereby anaesthesia was induced in each case with thiopentone 2.5% solution in doses of 4 mg/kg body weight. In addition, patients in group II received 50 mg of pethidine intravenously, while fifty in group three received 10 mg metoclopramide intravenously, just before induction of anaesthesia. Both drugs (pethidine and metoclopramide) were diluted to 20 ml with normal saline and were then given slowly. After ensuring sleep, each patient was then put in lithotomy position to facilitate surgery.

Maintenance

In group one, the patients were further divided into three equal subgroups of a hundred, and on each subgroup, either diethyl-ether, halothane or trichloroethylene in nitrous oxide and oxygen (2:1) was used to maintain the level of surgical anaesthesia while in pethidine and anti-emetic groups anaesthesia was maintained with diethyl-ether in 6 litres of nitrous oxide and 3 litres of oxygen (see Tab. I).

Patients were then allowed to breathe spontaneously through a mask and a Magill semiclosed circuit (Mapleson A) on a Boyle's machine. Halothane was administered from a floutex Mark III vapouriser, while diethyl-ether and trichloroethylene were administered from ether and trilene Boyles bottles respectively. Oropharyngeal airways were not used. Oral suction was carried out only in cases of excessive salivation interfering with breathing and in cases where vomiting actually occurred. Respiration was monitored by watching the reservoir bag for adequate and regular respiratory excursions and chest expansion. Breath-holding, coughing and hiccoughing were noted and managed by either assisted ventilation with gentle squeezes of the reservoir bag, or by low doses of intravenous thiopentone; until regular respiratory excursions were achieved.

Intravenous ergometrine in doses of 0.5 mg was given to every patient either on request by the surgeon or at the end of the operation. Patients assessed to have lost more than 200 ml of blood during the operation and those who needed either a repeat dose of ergometrine or syntocinon drip to achieve haemostasis, were all disqualified from the study. Each patient was then allowed to breathe pure oxygen for one minute at the

end of the operation. Another one minute later, the patient's condition was assessed as awake, safe or unsafe. Unsafe referred to any patient who vomited while on the operating table and therefore required closer post-operative observation. Duration of anaesthesia and surgery were then recorded.

2.3 POST-OPERATIVE PERIOD

During the recovery, blood pressure was taken in each case every fifteen minutes until the patient could answer questions intelligently. The lowest mean blood pressure during this period was noted in group III/anti-emetic group. Differences in the mean pre-operative and post-operative blood pressure measurements were recorded as mild-drop (0-12 mmHg) moderate drop (21 - 40 mmHg) or severe drop (41⁺ mmHg) (24,26,27).

All were followed for a maximum of six hours (12,24) after which they were allowed to receive visitors, eat or were discharged. During this period, following Riding's criteria (28) that "any nausea, retching or vomiting occurring after the operation whether remembered or not", and by asking the nursing staff, the presence of vomiting or retching or both, were carefully noted. Nausea being a subjective entity and therefore difficult to assess, was not recorded. Recordings were carried out in the recovery ward during the first post-operative hour and

subsequently on the ward for another five hours. All patients were transferred back to the emergency gynaecological ward after recovery from anaesthesia. Since grading of severity of symptoms depend on the assessor, in this study, in order to minimise confusion in the recordings, this was not done.

2.4 ANALYSIS OF DATA

The incidences (per cent) of vomiting in the three study groups were calculated and results compared using the standard chi-square-test. For purposes of this analysis retching was considered as vomiting. Because of inherent subjectivity, nausea alone was discounted. The anti-emetic effectiveness of the two drugs was compared using the standard chi-square-test. The relative significance of the effect of the two drugs (metoclopramide and Rodavan) on blood pressure was evaluated using the paired t-test.

FIGURE I

PROFORMA

PART I

NAME:		I.P. NO
AGE:		WEIGHT
TRIBE		OPERATION
SINGLE/MARRIED		NO. OF CHILDREN....
PREVIOUS ANAESTHESIA	YES/NO	VOMITING YES/NO
PREMEDICATION		DOSE
TIME GIVEN		PRE-OPERATIVE BP. mmHg supine

PART II

INDUCTION

THIOPENTONE	DOSE
OPERATION	START. END_

ROUGH ESTIMATE OF DURATION OF ANAESTHESIA

MAINTENANCE

TRICHLOROETHYLENE	2%		
HALOTHANE	0.25%, 0.5%, 1%, 1.5%, 2%, 2.5%		
DIETHYL-ETHER	2%	ERGOMETRINE	0.5 mg
N ₂ O	L/minute	PETHIDINE	50 mg
O ₂	L/Minute	METOCLOPRAMIDE	10 mg
		RODAVAN	2 tablets
		SYNTOCINON	DRIP

PART III

POST OPERATIVE RECORDING

1.

B.P.

TIME

2.	VOMITING	YES/NO	RETCHING	YES/NO
	NAUSEA	YES/NO		
3.	TIME OF FIRST FEED			

TABLE I

DRUGS GIVEN IN PREMEDICATION, INDUCTION
AND MAINTENANCE BY PATIENT GROUPS

GP	NUMBER OF PATIENTS		PREMEDICATION	INDUCTION	MAINTENANCE	SCIENCE
					Inhalational agent	N ₂ O:O ₂
I Incidence	300	100	Atropine 0.6 mg.	thiopentone 4 mg/kg	Diethyl- ether	Yes
		100	!1	11	Halothane	Yes
		100	!1	11	Trichloro- ethylene	Yes
II Pethi- dine		20	11	11	Diethyl- ether	Yes
III Anti- emetic	100	50	atropine 0.6 mg. + 2 tabs Rodavan	11	Diethyl- ether	Yes
		50	atropine 0.6 mg.	thiopentone 4 mg/kg and 10 mg meto- clopramide		

TABLE II

POST-OPERATIVE VOMITING INCIDENCE BY
 INHALATIONAL AGENTS IN GROUP I

Inhalational agent	Total no. of patients	Total no. vomiting	
		Total no.	incidence
Diethyl-ether	100	17	11%
Halothane	100	10	10%
Trichloro-ethylene	100	9	9%
All agents	300	36	12%

The differences between vomiting incidences were not significant.

2

1. Comparing diethyl-ether and halothane ($X^2 = 2.1$ $P > 0.1$).

2. Comparing diethyl-ether and trichloro-ethylene

($X^2 = 2.82$, $P > 0.05$).

t

TABLE III
 POST-OPERATIVE VOMITING INCIDENCE BY AGE GROUP
 AND BY INHALATIONAL AGENTS USED IN
 GROUP I

AGE GROUP	DIETHYL-ETHER			trichloroethylene			halothane			Total		
	Tot. no	No. vomit	incidence	Tot.	No. vomit	incidence	Tot.	No. vomit	incidence	Tot.	No. vomit	incidence
10-19	28	4	14.31	15	0	0	10	1	10%	53	5	9.4%
20-29	54	8	14.81	62	5	8.1%	69	6	8.7%	185	19	10.8%
30-39	13	3	231	17	3	17.6%	16	3	18.8%	48	9	19.6%
40-49	5	2	401	6	1	16.7%	5	0	0	16	3	18.8%
All ages	100	17	m	100	9	9%	100	10	10%	300	36	12%

TABLE IV

VOMITING INCIDENCE IN
DIETHYL-ETHER AND PETHIDINE GROUPS

ANAESTHETIC TECHNIQUE	TOTAL NO. OF PATIENTS	TOTAL VOMIT	INCIDENCE
Diethyl- ether	100	17	17%
Diethyl- ether + Pethidine	20	1	5%

The difference in incidence was not significant

($\chi^2 = 1.85$, $p > 0.1$).

TABLE V

POST-OPERATIVE VOMITING INCIDENCE
IN DIETHYL-ETHER AND ANTI-EMETIC
GROUPS

DRUGS GIVEN	TOTAL NO. OF PATIENTS	TOTAL VOMIT	INCIDENCE
Diethyl-ether alone	100	17	17%
D-ether+Rodavan	50	5	10%
D-ether+ Metoclopramide	50	5	10%

Reduction in incidence of vomiting from 17% to 10%
in either group was not significant (χ^2 ? nq p)

TABLE VI

MEAN BLOOD PRESSURE MEASUREMENTS BEFORE AND AFTER OPERATION
IN PATIENTS WHO HAD RECEIVED RODAVAN 2 TABLETS

MEAN PRE-OPERATIVE BLOOD PRESSURE	MEAN POST-OPERATIVE BLOOD PRESSURE	DIFFERENCE
83.3 mmHg	76.7 mmHg	6.6 mmHg
73.3 mmHg	86.7 mmHg	-13.3 mmHg
86.7 mmHg	80 mmHg	6.7 mmHg
76.7 mmHg	86.7 mmHg	-10.0 mmHg
83.3 mmHg	93.3 mmHg	-10.0 mmHg
73.3 mmHg	80 mmHg	- 6.7 mmHg
86.7 mmHg	80 mmHg	6.7 mmHg
66.7 mmHg	86.7 mmHg	-20.0 mmHg
83.3 mmHg	80.0 mmHg	3.3 mmHg
83.3 mmHg	60.0 mmHg	23.3 mmHg
90.0 mmHg	86.7 mmHg	3.3 mmHg
86.7 mmHg	86.7 mmHg	0 mmHg
83.3 mmHg	83.3 mmHg	0 mmHg
90.0 mmHg	100.0 mmHg	-10 mmHg
83.3 mmHg	73.3 mmHg	10 mmHg
73.3 mmHg	73.7 mmHg	- 0.4 mmHg
86.7 mmHg	110 mmHg	-23 mmHg
86.7 mmHg	76.7 mmHg	10 mmHg
93.3 mmHg	83.3 mmHg	10 mmHg
83.3 mmHg	76.7 mmHg	6.6 mmHg

.cont.

TABLE VI (cont.)

MEAN PRE-OPERATIVE BLOOD PRESSURE	MEAN POST-OPERATIVE BLOOD PRESSURE	DIFFERENCE
93.3 mmHg	83.3 mmHg	10 mmHg
83.3 mmHg	86.3 mmHg	- 3.0 mmHg
90.0 mmHg	113.0 mmHg	-23.0 mmHg
90.0 mmHg	103.0 mmHg	-13.0 mmHg
83.3 mmHg	83.3 mmHg	0 mmHg
83.3 mmHg	80.0 mmHg	3.3 mmHg
86.7 mmHg	86.7 mmHg	0 mmHg
96.7 mmHg	80.0 mmHg	16.7 mmHg
83.3 mmHg	86.7 mmHg	- 2.4 mmHg
83.3 mmHg	83.3 mmHg	0 mmHg
76.7 mmHg	76.7 mmHg	0 mmHg
73.3 mmHg	83.3 mmHg	-10 mmHg
73.3 mmHg	76.7 mmHg	- 2.4 mmHg
86.7 mmHg	80.0 mmHg	6.7 mmHg
80.0 mmHg	80.0 mmHg	0 mmHg
73.3 mmHg	80.0 mmHg	- 6.7 mmHg
93.3 mmHg	86.7 mmHg	6.6 mmHg
83.3 mmHg	76.7 mmHg	6.6 mmHg
83.3 mmHg	76.7 mmHg	6.6 mmHg
83.3 mmHg	83.3 mmHg	0 mmHg

...cont.

TABLE VI (CONT.)

MEAN PRE-OPERATIVE BLOOD PRESSURE	MEAN POST-OPERATIVE BLOOD PRESSURE	DIFFERENCE
96.7 mmHg	86.7 mmHg	10.0 mmHg
73.3 mmHg	83.3 mmHg	-10.0 mmHg
93.3 mmHg	100 mmHg	-6.7 mmHg
83.3 mmHg	83.3 mmHg	0 mmHg
60.0 mmHg	73.3 mmHg	-13.3 mmHg
83.3 mmHg	90.0 mmHg	-6.7 mmHg
80.0 mmHg	103.3 mmHg	-23.3 mmHg
86.7 mmHg	93.3 mmHg	-6.6 mmHg
83.3 mmHg	93.3 mmHg	-10.0 mmHg
86.7 mmHg	83.3 mmHg	3.4 mmHg

X = -1.56 P > 0.1

X = mean

SD = 10.10

SD = standard deviation

t = -1.09

t = t value for paired t test.

TABLE VII

MEAN BLOOD PRESSURE MEASUREMENTS BEFORE AND AFTER OPERATION IN PATIENTS WHO HAD RECEIVED METOCLOPRAMIDE 10 MG

MEAN PRE-OPERATIVE BLOOD PRESSURE mmHg	MEAN POST-OPERATIVE BLOOD PRESSURE mmHg	DIFFERENCE mmHg
73.3	70	3.3
80	73.3	6.7
86.7	73.3	13.4
73.3	76.7	-3.4
113.3	86.7	26.6
103.3	96.7	6.6
83.3	96.7	-13.4
83.3	83.3	0
86.7	86.7	0
73.3	73.3	0
83.3	73.3	10
86.7	83.3	3.4
86.7	66.7	20
86.7	73.3	13.4
96.7	83.3	13.4
103.3	83.3	20.0
66.7	63.3	3.4
83.3	76.7	6.6
73.3	73.3	0
83.3	73.3	10
93.3	83.3	10

.../cont.

TABLE VII (CONTQ)

MEAN PRE-OPERATIVE BLOOD PRESSURE mmHg	MEAN POST-OPERATIVE BLOOD PRESSURE mmHg	DIFFERENCE
86.7	73.3	13.4
96.7	73.3	23.4
80.0	73.3	6.7
83.3	73.3	10.0
103.3	110	-6.7
73.3	70	3.3
73.3	70	3.3
73.3	93.3	-20.0
86.7	60.0	26.7
93.3	83.3	10.0
93.3	66.7	26.6
76.7	70.0	6.7
76.7	73.3	3.4
76.7	70.0	6.7
73.3	63.3	10
70.0	63.3	6.7
73.3	63.3	10
76.7	73.3	3.4
86.7	73.3	13.4

.../cont.

TABLE VII fcQNT.1

<i>j</i>	<i>MEAN PRE-OPERATIVE BLOOD PRESSURE (mmHg)</i>	<i>/ /</i>	<i>MEAN POST-OPERATIVE BLOOD PRESSURE (mmHg)</i>	<i>j</i>	<i>DIFFERENCE</i>
	66.7		56.6		10.1
	66.7		63.3		3.4
	90.0		70.0		20.0
	86.7		76.7		10.0
	83.3		73.3		10
	93.3		93.3		0
	73.3		73.3		0
	93.3		86.7		6.6
	60		70.0		-10
	73.3		70.0		3.3

X = 7.21

P 4, 0.001

X - mean

S = 9.44

SD - standard deviation

t = 5.38

t - t value for paired
t test.

TABLE VIII
COMPARISON OF THE MEAN
BLOOD PRESSURE MEASUREMENTS IN
RODAVAN AND METOCLOPRAMIDE GROUPS

	Rodavan	Metoclopramide
Sample size	50	50
1 Mean	$\bar{X} =$	$\bar{X} - 1$
Standard deviation <i>i</i>	SDR=10.1	SD _n = 9.44

$$t = 4.47, \quad P \hat{=} 0.001$$

Hypotension in patients who received metoclopramide was significant.

TABLE IX

POST-OPERATIVE VOMITING INCIDENCES OBTAINED BY DIFFERENT
WORKERS SINCE 1957 BY ANAESTHETIC GIVEN

	1957 Burtles et al	1959 Smessart et al	1960 Riding	1961 Belville et al	1963 Haumann et al	1965 Heal et al	1965 Holmes: Odunt ⁿ et al	1970 Vance et al	1973 Vance et al	1981 author
Diethyl-ether	33%	23%		16.5%			35.6.%	10.4%		17%
Trichloro- ethylene	261				37%			15%		9%
Halothane					4.5%	40%		3.7°*		10%
Thiopentone N20: 02	181	14.5-30%	11.5%							
TOTAL	321	29%	11.5%	18%	21.3%		35.6% 1	5.1°*	21.2%	12%

Apomorphine, morphine, copper sulphate
Inhalational anaesthetic agents, antiemetics

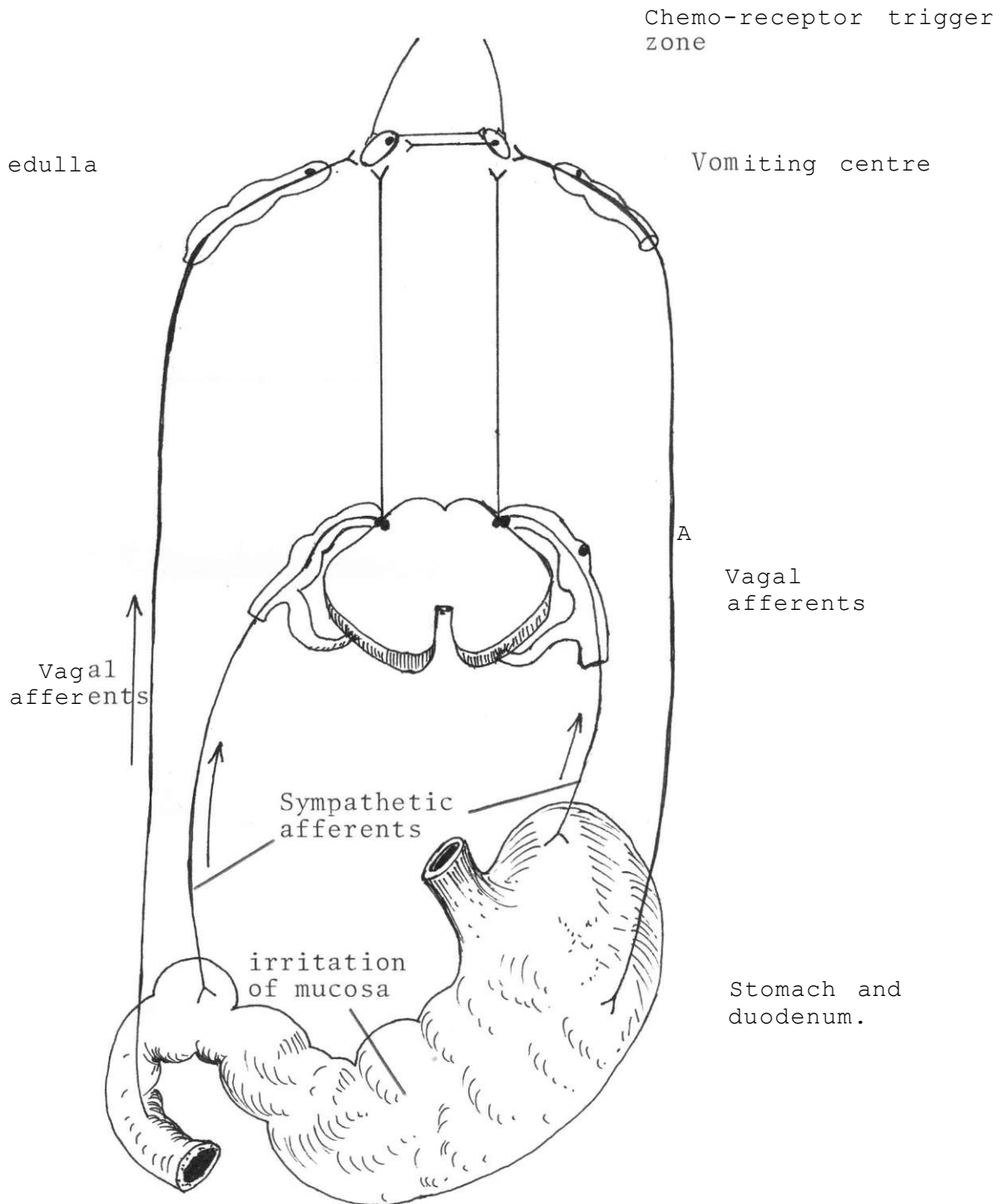
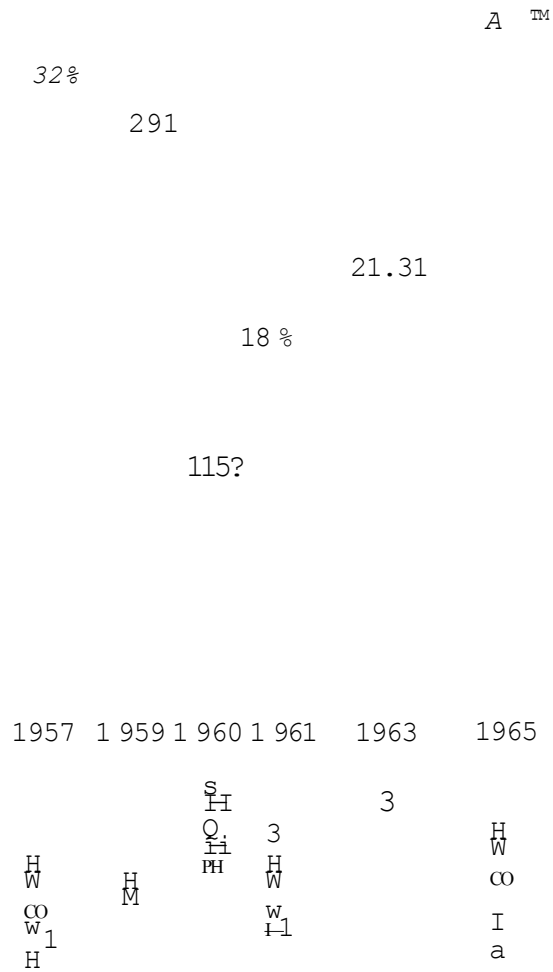
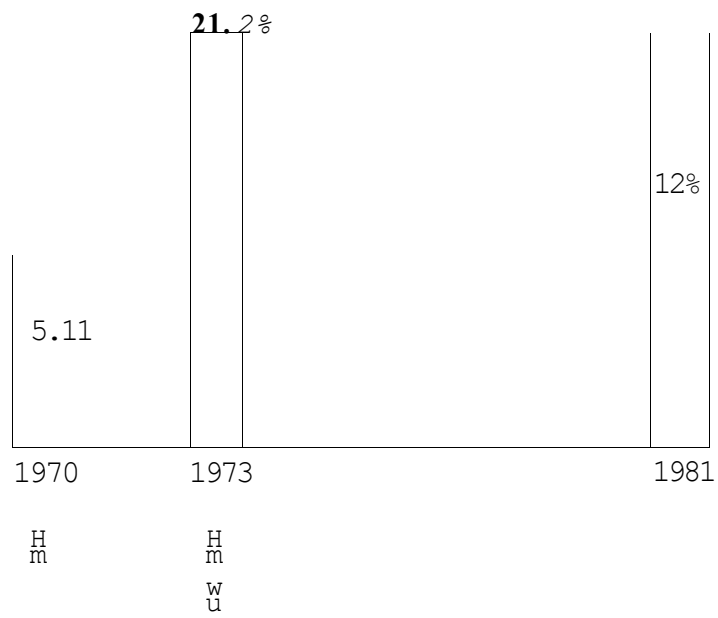


Fig II. Afferent pathways for the vomiting reflex, showing the chemoreceptor trigger zone, and the vomiting centre in the medulla.

FIG III
OVERALL INCIDENCES OF
WORKERS SINCE 1957



VOMITING BY DIFFERENT



3. RESULTS

Duration of anaesthesia varied from 3 - 15 minutes with an average of 6 minutes. Patients age varied from 15 - 49 years with a mean age of 25.5 years. Vomiting was noticed to occur most in the first post-operative hour.

3.1 INCIDENCE

Table II displays results of incidence of vomiting attributable to each of the three inhalational agents used. Diethyl-ether gave the highest incidence 171 compared to halothane 10% and trichloroethylene 9%. However on further evaluation the differences were found not to be statistically significant (comparing diethyl-ether and halothane $\chi^2 = 2.1$, $P > 0.1$; comparing diethyl-ether and trichloroethylene $\chi^2 = 2.82$, $P > 0.05$). Vomiting amongst patients in diethyl-ether group was associated with retching and in 501 of cases it tended to start during the operation. Excessive salivation, breath-holding, coughing and hiccoughing were common observations during diethyl-ether anaesthesia. Assisted respiration in form of gentle squeezes on the breathing bag eliminated breath-holding, coughing and hiccoughing. Unlike patients in the halothane and trichloro-ethylene groups, half the number in diethyl-ether group required oro-pharyngeal suction during surgery. This was necessary to clear the

airway of either or both excessive saliva and vomitus. At the end of the operation, more than 50% of patients in diethyl-ether group were graded as unsafe. Vomiting was noted to increase with advancing age, however, very few patients above the age of 30 years were anaesthetized with diethyl-ether (table III). There was no difference between pre-operative and post-operative blood pressure measurements. All patients were awake within the first hour, after which were transferred to the ward. None was recorded as vomiting while in the ward.

Ten out of a hundred patients in the halothane group were recorded as vomiting during the first post-operative hour. Unlike with diethyl-ether, vomiting in this group occurred much later; and was not associated with retching. Nausea though unrecorded was not common. Although 1% halothane in six litres of nitrous oxide and 3 litres oxygen was used, several patients required a repeat dose of oxytocin to control bleeding and abdominal pain was a common complaint post-operatively. Recovery was fast in this group so that half the number were graded as awake after one minute.

In trichloroethylene group, 91 of the patients vomited during the first hour. Retching was uncommon. Like halothane group, nausea was rare. Breath-holding as manifestation of light anaesthesia was common and was managed with either thiopentone in doses of 25 -100 mg or

trace of halothane (0.251). Vomiting in this group was noticed to increase with advancing age. More than 801 of the patients were graded as safe at one minute. Abdominal pain was not a common complaint in the post-operative period. There was no significant change in blood pressure measurements taken post-operatively compared to pre-operative measurements.

All groups combined gave an overall incidence of 12%. Vomiting was commonest among patients aged between 30-49 years.

3.2 PETHIDINE GROUP

The incidence of vomiting was not increased by giving 50 mg. pethidine prior to induction of anaesthesia (Table IV). However, the number of patients studied was very small (20) compared to the control (100). Although the drug was diluted to 20 mis with normal saline and given slowly a transient mild drop in blood pressure was observed three minutes after its administration. Breath-holding, coughing and hiccupping which were common findings in diethyl-ether group, were uncommon in this group. After 1 minute assessment revealed most of the patients were safe. All patients were awake within the first hour of post-operative period.

3.3 ANTI-EMETIC GROUP

Both drugs metoclopramide and Rodavan reduced the incidence of vomiting from 17% in the diethyl-ether group to 10% in either antiemetic group (Table V). The reduction in incidence however, was not statistically signi-

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ficant ($X = 2.09$, $P > 0.1$). Unlike metoclopramide, Rodavan administration did not alter initial blood pressure measurements (Table VI, VII). A mild to moderate drop in blood pressure observed in patients who received metoclopramide was significant ($t = 4.47$, $P \leq 0.001$) (Table VIII). None of the two drugs prolonged recovery time.

4. DISCUSSION

Vomiting, unlike regurgitation is an active process preceded by nausea, excessive salivation, pallor and sweating. The act involves closure of the glottis preventing aspiration of vomitus into the trachea. The breath is held in mid-inspiration. The muscles of the abdomen contract increasing abdominal pressure which eventually forces the cardiac sphincter to relax resulting into reverse oesophageal peristalsis with ejection of abdominal contents to the exterior.

Regurgitation which is a passive process, can also occur during anaesthesia especially if the cricopharyngeus muscle is relaxed with either deep anaesthesia or muscle relaxants in patients with hiatus hernia. Control of vomiting is by two centres: the vomiting centre and the chemo-receptor trigger zone, all situated in the medulla. The latter acts as a receptor for most impulses while the former acts as an integrator. Vomiting will result if either or both centres are stimulated. The stimuli include: psychological in form of sight, smell peculiar to the person, reflex abdominal stimulation by irritants, vestibular disturbance and central emetics. Impulses from gastrointestinal irritation are relayed from the mucosa to the vomiting centre over visceral afferent pathways in the sympathetic fibres and vagi (Fig II)- Studies show that bilateral ablation of the chemo-receptor trigger zone rendered

dogs refractory to 3 - 6 times the threshold emetic dose of cyclopropane (29) and abolished the emetic response to intravenous and cardiac glycosides without changing responsiveness to oral copper-sulphate (30). It is most likely that vomiting due to inhalational agents originates from the chemo-receptor trigger zone, while most anti-emetic drugs might be exerting their primary effect on this centre.

Inhalation of gastric contents may occur during vomiting or regurgitation. Patients on pethidine, morphine and atropine accentuated by emotional tension, pain and abdominal swelling including pregnancy, are more prone as all tend to have delayed stomach emptying. When inhalation of gastric contents occurs, it may cause cardiac arrest, severe bronchospasm with hypoxaemia, pulmonary and circulatory collapse (3,4,31). Wynne et al (31) studied factors that determine the prognosis after aspiration of vomitus. They found that P.H. of 2.5 was vital, and the quantity, content and distribution of vomitus within the lung all contributed to the prognosis.

Mendelson's syndrome, once developed, its management is still not satisfactory. Knowledge of the pathophysiology of the condition and facilities available for resuscitation are some of the factors that determine the prognosis. Therefore, in developing countries where trained personnel are few and facilities for resuscitation limited, ways of preventing occurrence of the Mendelson's Syndrome and the like, should be explored.

Over the years, post-operative vomiting has been studied extensively (32, 33, 28, 30, 34 -37, 8) but most of this work has been done in Caucasians (37). Results obtained in this study are compared with what had been done previously by different workers (see tab. IX and Fig. III). Although it (post-operative vomiting) is widely studied, few workers are quoted in this study due to limited literature on the subject.

In Table IX, diethyl ether gives the highest incidence followed by trichloro-ethylene, then halothane and lastly thiopentone. In Fig III, marked discrepancies amongst figures obtained by different workers on post-operative over-all incidence of vomiting are well displayed. Factors which are likely to account for such discrepancies include: age, sex and type of patient, type of premedication given, anaesthetic technique used, criteria used to define nausea and vomiting, closeness of observations, and length of period within which observations were taken (30, 32,33, 36, 37, 38).

Since there are many factors that tend to influence the incidence of vomiting, in this study, an attempt was made to control some of them. All patients were Grade one females, majority of whom had been pregnant, and had had a recent incomplete abortion. It is well known that females vomit more than males (30,32,39,37) and that early pregnancy and dilatation of the cervix whether

spontaneous or induced predispose easily to vomiting. The operation was either evacuation of the uterus and/or dilatation and curettage lasting for an average period of 6 minutes. A high incidence of vomiting after evacuation of the uterus especially if the cervix has been dilated was reported by Dundee et al (25). All patients in this study were induced with thiopentone 4 mg/Kg body weight which is known to be associated with a low incidence of vomiting (32, 33, 38). Burtles et al (32) commented on reduction in the incidence of vomiting after introduction of ultra-short acting barbiturates in 1930's. In their study, these workers obtained an incidence of 18% in the thiopentone group which was much less than in cyclopropane (24%) or trichloroethylene (26%) or diethyl-ether (33%) groups. Smessart et al (33) obtained an incidence of 14 - 30% in thiopentone group which was much lower than that of cyclopropane (24 - 50%) or diethyl-ether (23.3%) groups. Gold (38) in 1969 reached a similar conclusion. In his study, patients were premedicated with quinalbarbitone and anaesthetised with different anaesthetic agents: he obtained the lowest incidence in the thiopentone group and concluded that the presence or absence of thiopentone as an induction agent played a major role in the overall incidence.

All the patients in this study were operated on in lithotomy position which is likely to encourage regurgitation.

Burtles et al (32) and Gold (38) found that this position was not associated with vomiting and when compared to trendlenburg or reverse trendlenburg it gave less incidence of vomiting than the latter two. Oropharyngeal airways which tend to cause irritation with subsequent coughing and vomiting (40) were avoided in all cases. Oral suction during anaesthesia was avoided as much as possible and was necessary only in diethyl-ether group, whereby, excessive salivation became a nuisance or where vomiting actually occurred. Oropharyngeal suction is known to stimulate the vomiting reflex.

We tried to prevent hypoxia by giving 30% oxygen during operation and 100% oxygen for one minute at the end of the procedure. Since nausea is difficult to define, it was not recorded in this study. Vomiting defined as an active ejection of stomach contents through the mouth, and retching defined as straining with or without ejection of stomach contents, were recorded. In the retching group of patients, most ended up vomiting while a few did not. Therefore all were recorded as vomiting. Ergometrine was given to all. All patients were followed for a maximum of 6 hours after which they were allowed to receive visitors, eat or were discharged. Dundee et al(25) noted that the above two factors (visitors and food) contributed to vomiting especially if patients were followed for more than six hours.

Oduntan et al (37) obtained an overall incidence of 5.1% in Nigerian Africans and concluded that there may be a racial difference in the aetiology which might account for the low incidence they obtained compared with what had been obtained in Caucasians. They used all grades of patients of both sexes. Their patients were followed for only three hours. In this study an overall incidence of 12% was obtained in females, which is much lower than what had been obtained in Caucasians by other workers. Burtles et al (32) reported an incidence of 32%, Smerssart et al (33) 29%, Haumann et al (34) 21% and Vance et al (8) 21.2%. Burtles et al worked on a control group of 1702 patients. This group, however, consisted of all age groups including children and both sexes. Most of their patients received morphine, papaveretum and pethidine without any antisialogogue. The patients were scheduled for general surgery and therefore might have had systemic physiological and biochemical disturbances. Smerssart et al (33) obtained an incidence of 29% in a group containing both sexes. Factors pointed out in the study done by Burtles et al are the same factors applying to the study done by Smessart et al. Haumann et al (34) working on a hundred and thirty females undergoing either dilatation and curettage or cystoscopy, obtained an incidence of 21%. However, the number of patients in their study groups was small. Dundee et al (25)

stressed the importance of having a large number of patients in a group so that factors of unknown importance, like motion sickness (32) can be minimized. Vance et al(8) working on plastic surgical patients obtained an incidence of 21.21. Their patients were premedicated with 25 mg pethidine, promethazine and atropine which drugs, are said to decrease vomiting (30, 32, 15, 26). However, their study group comprised of both sexes, all age groups and all underwent head and neck surgery. In this study a low incidence of vomiting was obtained in the control group. This could have been due to the fact that all patients were

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African females (37) premedicated with atropine (15,37,26), induced with thiopentone (32,33,38), and were undergoing brief surgical procedure (32,33,38). Their post operative follow up was limited to a maximum period of six hours (25).

Considering inhalational agents, in this study, diethyl-ether anaesthesia was associated with the highest incidence of vomiting. Although this was not significantly higher than either halothane or trichloroethylene (Table II), similar results (high incidence of vomiting) had been reported by Burtles et al (32), Smerssart et al (33) and Oduntan et al (37). Holmes (36) however, working on two hundred and fifteen patients anaesthetized with either diethyl-ether or other anaesthetics noticed no difference in vomiting incidence obtained in either groups.

Trichloroethylene was found to give a higher vomiting incidence than halothane (34,37). In this study, no significant difference was found between the two groups

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($X = 0.066$ $P > 0.7$). Patients anaesthetized with trichloroethylene however, required either small doses of thiopentone (25-100mg) or a trace of halothane (0.25%) to maintain sleep during the operation. Probably the two agents added (halothane and thiopentone) which are reported to possess slight antiemetic property could have contributed to the low incidence obtained in trichloroethylene group. Thiopentone and its contribution to the incidence of vomiting has already been discussed (32,33,38). Results obtained from studies done to evaluate the anti-emetic effect of halothane are rather controversial. Rajagopalan et al (41), while working on a group of females undergoing dilatation and curettage, obtained a lower incidence of vomiting in halothane group than trichloroethylene group. They however stated that it was fundamentally wrong to ascribe an anti-emetic property to a volatile anaesthetic agent. Haumann et al (34) working on patients anaesthetised with trichloroethylene, nitrous oxide and oxygen observed a decrease in the incidence of post operative vomiting when halothane 1% was substituted for trichloroethylene for the last five minutes. They therefore concluded that halothane might have an anti-

emetic effect. Gold (38) got a lower incidence of vomiting in halothane group than either cyclopropane or diethyl-ether. Heal (35) and Holmes (36), however, observed no difference in the overall incidences obtained after using halothane or any other anaesthetic agent. Ratra et al(21) working on females undergoing minor gynaecological operations and anaesthetised with thiopentone, nitrous oxide and oxygen, observed no significant change in the incidence after administration of halothane 11 for the last five minutes. Oduntan et al (37) also noted no significant difference in the incidence after chloroform, halothane or thiopentone nitrous oxide, oxygen and relaxant techniques.

Age and weight are some of the factors, within the patient, that influence uptake, distribution, metabolism and excretion of drugs. Dundee et al (24) stressed the value of a narrow age limit in a study, as varied age limit influences the incidence of vomiting remarkably (32,33, 37, 39). Burtles et al (32) found that vomiting was common during the first and second decades of life, after which it decreased with advancing age. Haumann et al(34) noted a decrease in the incidence of vomiting in patients at extremes of age, and that children between the age of 0-9 years showed the highest incidence. Oduntan et al (37) working on all age groups, found vomiting at its peak between

second and third decades. In a study done by Janhunen et al (39), they found that women aged between 40-49 year vomited more than any other age group. Morrison et al (2) statistically demonstrated that the use of at least a hundred patients in a study group, ruled out any discrepancies likely to arise in results if a drug is given based on either body weight basis or on a fixed-dose basis. In this study, a gradual rise in incidence of vomiting with advancing age was observed as shown in table III. However, most patients who presented for these gynaecological procedures were aged between 15 - 39 years.

Dilatation and curettage is a very painful procedure requiring deep levels of anaesthesia and analgesia in order to prevent unwanted effects such as laryngospasm and vasovagal shock (42,43) which sometimes do occur during this procedure. However, deep levels of anaesthesia in such brief operations are unwanted, time consuming, and are associated with high incidence of vomiting (37). Some workers recommend local analgesia in form of paracervical block or extradural block (42), but the two procedures also carry their own unwanted effects. Some anaesthetists prefer to include opiate analgesics in their anaesthetic technique either as premedicants or in post-operative medication. Results from studies done on opiates when included in

anaesthetic technique used, are rather controversial. Some workers observed an increase in the incidence of post-operative vomiting (28,30,34,26,13,15) while others noticed no change (39,37). Riding (28) while working on a group of unpremedicated females noted that the addition of 10 mg morphine to the anaesthetic technique he used, increased an initial incidence of vomiting of 22.4% to 66%. Bellville et al (30) found that vomiting was more associated with morphine than pethidine when either drug was used. They further noted that vomiting following pethidine administration tended to be common, when the drug was administered in doses of more than 1mg/kg body weight. Dundee et al (26) working on a group of fit females premedicated with pethidine, found that the incidence of vomiting increased markedly especially when used alone without either atropine or hyoscine. Dizziness, hypotension and prolongation of recovery time were some of unwanted effects they observed. Clarke et al (13) used morphine 10 mg or pethidine 100 mg on females undergoing minor gynaecological procedures and maintained on the same anaesthetic technique. They found that the incidence of vomiting in the placebo group 18% was increased to 60% after morphine and to 64% after pethidine. Working on a similar group as above and using similar drugs, Dundee et al (15) reported an incidence of 50-60% after their administration. They further noted that vomiting amongst the

morphine group was more common and tended to occur much later than in the pethidine group. On the contrary, Janhunen et al (14) and Oduntan et al (37) in their studies found that addition of opiate analgesics did not influence the incidence of vomiting. In the present study, twenty patients were given a fixed-dose of 50 mg pethidine each, just prior to induction of anaesthesia, and of these only one patient vomited. A mild drop in blood pressure and otherwise smooth anaesthesia were observed in this group. However, a firm conclusion could not be drawn from such a small sample; Morrison et al (27) advises that a group of a hundred patients be used if a drug is to be administered on a fixed-dose basis. This gives results comparable to administration of the same drug on an individual weight-related basis.

Halothane is the commonest inhalational agent used at the Kenyatta National Hospital. During its administration, in order to prevent giving a hypoxic mixture, compressed gases (oxygen and nitrous oxide) are necessary. It is to be noted that halothane is expensive and unsafe in the hands of inexperienced anaesthetists. Its relaxant effect on a pregnant uterus has been studied extensively by several workers (44-46). Using 0.5% concentration, Moir (44) found that such a concentration had no effect on the myometrium. But Naftalin et al (45) using isolated pregnant uterine strips exposed to 0.5% halothane vapour for half an hour, demonstrated a 25% reduction in peak-developed isometric tension. However, Latta et al (46) found that

halothane arterial tensions decreased rapidly when the vapouriser was turned off. In the present study, a minimum of 1% concentration of halothane in 6L nitrous oxide and 3L oxygen was used in 100 patients in the incidence group to maintain surgical level of anaesthesia (Table II). This appeared to produce relaxation of the uterus as evidenced by repeated doses of oxytocic drugs which were necessary to aid haemostasis. Therefore its use in concentrations exceeding 0.5%, in evacuation of the uterus, should be discouraged. Trichloro-ethylene is cheap, has analgesic property and is non-irritant. However, it is a poor anaesthetic and rarely does one get more than 1.5% concentration when a Boyles bottle is used. Compressed gases are necessary in maintaining a concentration of 1.5%. Diethyl-ether, unlike halothane and trichloro-ethylene, is irritant and therefore associated with a high incidence of post-operative sickness. However, it is cheap, and can be administered without compressed gases using the E.M.O. (Epstein Macintosh Oxford) machine (47). In Uganda and some district hospitals in Kenya, it is still the commonest anaesthetic agent used. It is one of the safest agents in the hand of inexperienced anaesthetists and paramedicals. This is confirmed by what John Snow said in 1858 (48) that "I hold it therefore to be almost impossible that a death from this agent (ether) can occur in the hands of a medical man who is applying it with

ordinary intelligence and attention". Therefore, the use of diethyl-ether in developing countries where trained doctor anaesthetists are still few, is of much value. In this study, an attempt was made to evaluate the influence of pethidine (the commonest analgesic used in the Kenyatta National Hospital) and Rodavan, a new anti-emetic, on the post-operative sickness attributed to diethyl-ether.

A lot of work has been done on the role of anti-emetics in reducing the incidence of vomiting. Phenothiazine derivatives were probably the first to be widely studied (20,21,13,12,1,19) and are still some of the commonly used anti-emetics. Most of them possess a sedative effect and therefore tend to prolong the recovery period. Hypotension and extrapyramidal effects are some of their unwanted properties that lead to further searching for a better anti-emetic. Butyrophenones are effective anti-emetics (16,17,18,19) but nowadays are widely used as adjuncts to fentanyl and phenoperidine in neuroleptanalgesia rather than being used as anti-emetics. Domperidone, a potent synthetic anti-emetic and dopamine receptor antagonist has been tried in prevention and treatment of post-operative sickness (22,23). Its chemical structure portray both anti-emetic and prokinetic activities (23). Despite its lack of side effects (22,23) it seems not to be a popular drug.

Perhaps the most widely studied and used anti-emetic is metoclopramide. It was discovered in 1964 in France when Justin et al (49) working on orthochlor procainamide accidentally obtained methoxy-2-chloro-5 procainamide (metoclopramide). Further evaluation of its anti-emetic effect followed in 1967 after which it was tried in post-operative vomiting (9-15). It acts locally on the gut and centrally on the chemoreceptor trigger zone. Since fibres from the labyrinth tend to bypass the chemoreceptor trigger zone, its value in motion sickness is doubtful. It decreases gastric emptying time by promoting motility, therefore, it is a handy drug in emergency anaesthesia. It is available in oral and parental preparations. Although it seems an ideal drug, its action is brief especially when given intravenously. Therefore, repeated doses are necessary in prevention of vomiting due to morphine which tends to occur much later and is more prolonged than that due to pethidine. However, such repeated doses are associated with lassitude, drowsiness, urticarial rashes, and rarely extra-pyramidal effect (49). Sedation effect tend to prolong recovery which is an expensive exercise in terms of staff and room to accommodate patients, and also it delays mothers in the hospital. Rodavan which rarely gives sedation, was tried in this study. Both Rodavan and metoclopramide were administered on a fixed-dose basis to a group of a hundred patients.

Rodavan, a new anti-emetic, is made up of a combination of Chlorphenoxamine hydrochloride, 8 Chlorotheophylline and caffeine. Chlorphenoxamine hydrochloride is a compound of the benzhydryl ether group, and when combined with 8 chlorotheophylline, unlike metoclopramide, is effective in nausea and vomiting due to motion sickness. Caffeine counteracts the sedative component of Chlorphenoxamine without reducing the anti-emetic effect. Rodavan is available in tablets and suppositories only. In this study, 2 tablets of Rodavan were given to 50 patients, one and half hours before induction of anaesthesia. It was found to be as effective as intravenous metoclopramide in reducing post-operative vomiting (Table V). However the difference between the control and anti-emetic groups was ^{not} statistically significant ($X = 2.09$, $P > 0.1$). Unlike metoclopramide, hypotension was not observed in patients who received Rodavan (Table VI and VII). Hypotension observed in metoclopramide group was statistically significant ($t = 4.47$, $P < 0.001$). Therefore Rodavan appears a superior anti-emetic drug especially if it is given to patients who are already hypotensive. However, it is not available in injectable form, which tends to make it less useful in emergency anaesthesia.

CONCLUSIONS

Post-operative vomiting in Kenyan African females undergoing minor gynaecological operations appears not as common as in Caucasians. It is still however a problem (17%) when diethyl-ether (commonest inhalational agent used in Kenya and Uganda) is used. Rodavan (a new anti-emetic) was as effective as metoclopramide in reducing post-operative vomiting incidence from **11%** to **10%** following diethyl-ether anaesthesia. However, the drop in vomiting incidence in either case was not significant ($P > 0.1$). Either drug can be administered pre-operatively in an attempt to prevent the Mendelson syndrome. Caution is required in administering metoclopramide intravenously in patients who are already hypotensive. Of the two drugs, Rodavan appears safer especially in the hands of the unexperienced. Unfortunately, it is not available in injectable form and it is slightly more expensive than metoclopramide. If it has to be used, it should be given about one and half hours before anaesthesia

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