THE EFFECTS OF INJECTABLE METOCLOPRAMINE AND RANITIDINE ON THE HYDROGEN ION CONCENTRATION AND VOLUME OF GASTRIC ASPIRATES IN PATIENTS UNDERGOING EMERGENCY AND ELECTIVE CAESARIAN SECTION FOR THE PREVENTION OF ACID ASPIRATION SYNDROME.

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A DISSERTATION SUBMITTED IN PART FULFILMENT FOR THE DEGREE OF MASTER OF MEDICINE IN ANAESTHESIA, UNIVERSITY OF NAIROBI.

1988.

D E C L A R A T I O N.

THIS DISSERTATION IS MY ORIGINAL WORK AND HAS NOT BEEN PRESENTED FOR ANY DEGREE IN ANY OTHER UNIVERSITY.

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ACKNOWLEDGEMENTS:

I wish to express my sincere thanks and gratitude to the following.-

Dr. S.K. Kahuho for his supervision and guidance in writing this dissertation.

The Senior house officers in the Department of Obstetrics and Gynaecology for this cooperation and assistance during this study.

The Nursing Staff of Labour Ward and Maternity Theatre for their help and assistance both in material and moral form.

The Director, Kenyatta National Hospital for allowing me to undertake this study.

The Laboratory Staff of Microbiology Department for assisting me in the use of their laboratory.

To my wife Jaimala and children for their cooperation and encouragement during the period of this study.

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SUMMARY.

This study was carried on 160 adult patients who were undergoing emergency or elective caesarian section. They were divided into 4 equal groups of 40 patients each. All patients were classified as ASA 1 and ASA II

Group 1 did not receive any sedation. Group 11 received I.M. metoclopramide 10mg half an hour before surgery, group 111 were given I.M. ranitidine 50mg half an hour preoperatively and group IV received both I.M. ranitidine 50mg and I.M. metaclopramide 10mg half an hour before operation. All 160 patients were given I.V. Atropine 0.6mg during preoxygenation prior to induction.

After intubation and stabilization of the patients under standard procedures a nasogastric tube size 14 or 16 was passed orally into the stomach and all the gastric contents were removed. The volumes were noted and the pH determined both at induction and at reversal.

Results of the study showed that patients in group 1 (control) had a high mean gastric volume 37.5$\pm$ 3.89mls S.E.M. and a low mean pH 3.19$\pm$012 S.E.M. with 55% of the patient having gastric

aspirate volumes above 25mls and 57.5% of the patients having pH below 2.5.

A critical value of pH below 2.5 and a gastric volume of above 25mls has been determined to be the high risk factors in acid gastric aspiration syndrome. Patients receiving metoclopramide in group 11 did not show a significant change in pH values as compared to the control group but definitely had reduced gastric aspirate volumes of $10.23^{+}1.59$mls S.E.M. as compared to 37.5mls in group 1.

Ranitidine raised the pH above 2.5 in 97.5% of the patients in group 111 and also significantly reduced the gastric volumes to $9.08^{+}1.20$mls S.E.M.

The combination of ranitidine and metoclopramide did not show any particular superiority over ranitidine alone and the results between group 111 and 1V were comparatively the same.

Therefore injectable ranitidine with or without metoclopramide is effective in raising the pH above 2.5 in 97.5% of the patients and reducing gastric volumes below 25mls in 87.5% of the patients. None of the patients who received Ranitidine had a combination of pH below 2.5 and a gastric aspirate volume above 25mls in group 111 and 1V.

INTRODUCTION:

Acid aspiration syndrome is a serious condition which may follow the aspiration of gastric contents into the air passages, giving a clinical picture like that described by C.L. Mendelson (1) in 1946 as Cyanasis, dyspnoe, tachycardia, bronchospasm and in fulminant cases either acute oedema of the lungs with active respiratory failure. Solid food paricles in the air passage may cause death due to total obstruction or atalectasis due to partial obstruction of the airways.

Gastric contents are aspirated either during active vomiting or during silent regargitation. Active vomiting occurs during light planes of anaesthesia and is liable to be initiated by laryngoscopy, intubation, intermitent positive pressure ventilation by mask, hypotension, hypoxia and other factors. Vomiting is most likely to occur during induction or at reversal when the airway is not protected by an endotracheal tube and cuff. Regurgitation into the pharynx occurs when there are gastric contents lying in the oesophagus and the chicopharyngeal sphincter is relaxed by general anaesthesia, particularly when

the relaxant drugs are used. The tone of the lower oesophageal sphineter is also altered by most anaesthetic and premedication drugs.

Aspiration of acid gastric contents into the lungs produces an inflamatory reaction with a cellular exudate and loss of bronchial epithilium. The oedema fluid may be haemorrhagic. There is leucocyte infiltration and parancymal destruction. Alveoli are filled with hyline exudate and extravasated red cells. This above pathological picture is usually worse when the pH of the gastric contents is below 2.5 and the amount of gastric contents above 25mls. Death may occur from complete obstruction of the air passages by food paricles, or by the reaction produced by the acid aspirate, the cellular exudate which causes severe hypoxia due to a $\dot{V}/\dot{Q}$ mismatch and shunting of blood. This hypoxia may not be reversed inspite of intermittent high positive pressure ventilation with 100 percent oxygen.

The morbidity and mortality associated with aspiration of gastric acid contents is high, and one should undertake all measures to decrease the incidence and severity of the disease as a

phrophylaxis rather than a cure by applying all anaesthetic techniques to avoid regurgitation and active vomiting during induction and reversal. They are as follows:-

Antacids The prophylactic use of antacids before surgery seems to be a logical method of combating Mendelsons syndrome (10), the efficacy of antacids has however been questioned (11) and pulmonary aspiration of antacids alone especially the particulate may itself lead to severe pulmonary damage (12). Although antacids reduce acidity, being liquids they increase gastric volume, and they may even significantly prolong gastric emptying (13). Antacids also increase the serum gastrin levels and cause an acid rebound. Magnisium Tricilicate 10mls 10-15 minutes before induction has been used but being particulate is dangerous if aspirated. Sodium Tricilicate a non-particulate antacid which mixes well with the gastric contents 15 mls of 0.3m sodium citrate solution 5-15 minutes before induction can increase the gastric pH to greater than 3.0 in all patients (16).

Other antacids like colloidal aluminium hydrochloride failed to increase the pH above 2.5 in 12.5% of the patients (10).

Anticholinergic drugs inhibit the vagally mediated production of gastric juice thereby reducing gastric acid secretion and increasing gastric pH, but only to a highly variable degree.

H_2 receptor drugs. Ash and Schild (26) postulated the existence of H_2 receptors, activation of which stimulates the heart muscles and gastric secretion. The effects are blocked by H_2 receptor antagonist drugs like cimetidine and Ranitidine.

Ranitidine is a substituted amino-alkylfuran derivative which markedly inhibits basal and noctural gastric acid secretions as well as secretion stimulated by histamine and pontagastric. It is Rapidly absorbed after oral administration acheiving peak plasma levels after 60-90 minutes therapeutically effective plasma concentration last at least 8 hours which outlasts that of Cimetidine Most of the drug is excreted in the urine unchanged with an elemination half life of approximately 2 hours.

A single dose of 100mg of oral ranitidine inceases the pH to greater than 7.0 for 7 to 8 hours (34). There are no obvious side effects that would preclude the use of ranitidine as it does not inhibit drug metabolism by inhibiting the microsomal encyme systems.

Cimeditine is a weak imidazole base and peak blood levels are achieved 45 to 60 minutes after oral administration plasma half life is about 2 hours. It is excreated by the kidneys within 24 hours of oral adminitration. 48 to 77% of the drug being excreted unchanged, the rest of the cimetidine is excreted in the form of sulfoxide metabolites. Sulfoxide is a product of hepatic inactivation by convention of the side chain thioether. Unlike Ranitidine cimetidine has a number of side effects which are due to inhibition of drug metabolism, as it binds to microsomal p-450, suppresses bone marrow, decreases liver blood flow etc.

Factors affecting gastric emptying.

Starving for 6 to 8 hours reduces gastric volumes, but has little effect on pH which is acidic and there is a delay in gastric emptying especially due to emotional stress, pain, toxicity and the use

of narcotics, significant gastric volumes may be present and mechanical or pharmacological methods of stomach emptying may be employed.

Passage of a wide bore Nasogastric tube for evacuation by suction, digital stimulation of the pharynx by the patient can initiate vomitting in a fully awake patient. Apomorphine-a morphine derivative which is a powerfull stimulator of the chemoreceptor trigger zone is commonly used as an ematic.

Metoclopramide - a derivative of procainamide causes intensified gastric paralysis and dilatation of the pylorus, leading to gastric emptying it also increases the tone of the lower oesophageal sphincter.

Cricoid cartilage pressure at induction of anaesthesia lessens the risk of regurgitation and aspiration in these patients. In case of a difficult and failed intubation, employ the failed intubatiion drill and avoid hypoxia and repeated trails of laryngoscopy and intubation as this may initiate active vommiting, and subsiquent

aspiration of vomittus I.V. fluid is the choice for water and electrolyte balance and patients should not be given meals in labour ward. By avoiding narcotic analgesics pre operatively there will be no slowing of gastric emptying and the lower oesophageal tone will not be decreased. Better Apgar scores will be a result of all the above.

AIMS AND OBJECTIVES:

This study was undertaken to:-

1. Evaluate the basic pH and volumes of gastric contents on obstetric patients in Kenyatta National Hospital.

2. Evaluate the percentage of patients at high risk of acid aspiration syndrome.

3. Evaluate the efficacy of the H_2 receptor blocking agent -Ranitidine alone and in combination with Metoclopramide in the reduction of pH and volumes of gastric contents in patients coming in especially for emergency caesarian sections.

4. Make recommendations on ways of prophylaxis and practical labour ward management to reduce risk factors in patients prior to anaesthesia.

MATERIAL AND METHODS.

One hundred and sixty adult female inpatients scheduled for emergency caesarian section were studied. The protocol was approved by the ethical committee of our hospital and each patient's verbal consent was asked for. No patient in this study had any history of gastrointestinal disorders and neither were they on any drugs known to influence gastric acidity and volume. All patients were classified as ASA class I & II. None of the emergency patients were starved deliberately as they all came as emergencies. They were randomly allocated into four groups of forty patients in each group.

All patients were premedicated with intravenous atropine 0.6mg just prior to induction. Patients in group 1 received no additional premedication and served as controls. Group 11 patients received 10mg of metaclopramide intra-muscularly at least 30 minutes or more before induction. Patients in groups 111 received 50mg of ranitidine intramuscula

also 30 minutes or more prior to induction. Patients in group IV received both 10mg of metoclopromide and 50mg ranitidine intramuscularly 30 mins or more prior to induction of anaesthesia.

After satisfactory induction of anaesthesia and stabilization of the condition of the patient after tracheal intubation, a size 16 nasogastric tube was passed into the stomach and all available gastric contents were aspirated by suction into a 50ml syringe. The position of the gastric tube was verified by auscultation over the epigastrium during insufflation of small amounts of air via the nasogastric tube. The volume of gastric juice was measured by graduation on a measuring cylinder, while smaller amounts were determined in the syringe. The pH was determined using an Orion research pH meter model 301 with a pH sensitive electrode and an analog pH meter gauge. The pH was determined by laboratory personel who were not aware of the premedications administered. Before use, the pH meter was each time checked with standard buffer solutions of pH 4.0 and pH 7.1.

All patients received a set anaesthetic technique of preoxygenation 5 mins following induction with 5mg/kg sodium thiopenton and 1mg/kg succinycholine intravenously, cricoid pressure and intubation, followed by inflation of cuff and I.P.P.V. after giving intravenous pancuronium 0.8mg/kg maintenance with Halothane/O_2/N_2O I.P.P.V. using closed circuit system with CO_2 absorber with high flow rates. I.V. Ergometrine/Oxytoxin was given after clamping or cord. I.V. pethidine 0.1mg/kg after delivery. Neostigmine 2.5mg was given with atropine 1.2mg at reversal in each case.

Blood losses, apgar scores of the neonates, duration of operations and blood pressure changes and pulse rate changes were all recorded.

The pH Electrode.

pH is the negative logarithm of hydrogen ion concentration.

The S.I. unit defining the acidity or alkalinity of a solution is the hydrogen-ion concentration $[H^+]$. This is expressed in nanomoles per litre (nmol.($^-$1). However it is not possible to measure $[H^+]$ directly in aqueous solutions so that the acid-base state is usually defined by measuring the pH with a glass electrode. This electrode produces a voltage which is related to the

tendency for the hydrogen ions to escape from the solution. It thus measures the effective concentration or 'activity' of the hydrogen ions.

At 37°C. the glass pH electrode produces an electrical output of about 60mV per pH unit. The pH glass electrode is versatile, unaffected by the solution to be measured and can be used with suspension as well as solutions. The glass electrode assembly consists of two half cells (just as a battery consists of two half cells) each of which develop a potential when connected together. One of the reference half cell (commonly called the reference electrode) maintains a constant potential, whilst the other, the glass half cell (or glass electrode), develops a potential which is proportional to the concentration of hydrogen ions present.

The pH electrode is standardized by the use of buffers with known pH. e.g. Phosphate buffers of pH 6.835 and 7.386. The pH electrode is emersed in a

water bath to ensure that the electrode is at 37°C $\pm$ 0.1°C, or a correction and recalliburation is done to compensate for temperature difference.

RESULTS:

A total of 160 patients were studied and were randomly allocated into 4 groups of 40 patients each. Premedication and intra-operative drugs given are listed in table 1. As is evident from table 1 only the premedication varied between the 4 groups, all other intraoperative medications were similar. The patients mean age, heights and weights are indicated in table 2. The mean age of all patients was 24.1 years. The mean ages in the 4 groups did not vary much from one group to another ranging between 23 to 25 yrs. The mean height of all the patients was 5'2½" varying in the 4 groups between 5'2" and 5'3". Mean weight was 64.5kg in all 160 patients. The mean weights varied between 63 and 66kg in the 4 groups. It would therefore mean that the ages, heights and weights did not vary significantly in the 4 groups.

Table 3 shows the age distribution of the 160 patients. 87% of the patients were between the ages of 15 and 29 yrs. 11.3% of the patients had ages between 30 and 39 years. Table 4 shows a histogram of the age distributions. There were

no patients with an age below 15 years or above 45 years. Table 5 shows the variation of ages between the 4 groups of patients. There were some variations in the ages but most of the patients fell in the ages between 15 and 29 years. There was no significant deviation in the age distribution between the 4 groups.

Gastric pH characteristics are shown in table 6 indicating the mean pH value of control group 1 as pH 3.19 $\pm$ 0.21 S.E.M.ranging from 1.8 to 6.8. Patients with a pH below 2.5 were 57.5% while the patients in Group 11 receiving metaclopramide premedication had a pH mean $\pm$SEM of 3.47 $\pm$ 0.27 with a range of 1.8 to 7.8 with 45% of the patients having a pH of below 2.5. In contrast, patients in group 111 receiving I.M. Ranitidine 50mg had a mean pH as high as 6.03 $\pm$ 0.20 and a range of pH between 2.4 and 8.6 with only 2.5% of the patients having a pH of below 2.5. In group IV where patients were given both Ranitidine and metoclopramide as premedication the pH ranged between 2.2 and 8.4 with a mean pH of 5.73 $\pm$ 0.25 S.E.M. and 5% of the patients having pH below

2.5. It is evident from this statistical data that the control group 1 had a very low mean pH value with a high percentage of patients who fall under the high risk group of aspiration pneumonia being a pH of below 2.5.

Patients in group 11 receiving metoclapromide as premedication did not show much significant difference as compared to group 1 still having a low mean pH value of 3.47 ± 0.27 and pH ranging between 1.8 and 7.8. As high as 45% of the patients having a pH of 2.5 or below. Although metoclapromide had reduced the percentage of patients with pH values of below 2.5 from 57.5% to 45% as compared to group 1 patients, it is still not of significant value as far as prophylaxis of acid aspiration is concerned. In contrast group 111 patients who received i.m. Ranitidine 50mg had a high pH value ranging between 2.4 and 8.6 with only one patient out of 40 having a pH less than 2.5 and a mean pH value of as high as 6.03 ± 0.20 SEM.

Group lV patients who received both Metoclopramide and Ranititine did not show any advantage over group lll patients as far as pH is concerned having a mean pH of 5.73$^{+}_{-}$ o.25 SEM and a pH range between 2.2 to 8.4 with only 5% of the patients having pH less than 2.5.

Table 7 gives us the characteristics variations of gastric volumes between the 4 groups. Gastric volumes of the 25mls is considered as a risk of aspiration pneumonia. The patients in the control group 1 show a high mean gastric volume of as high as 37.5$^{+}_{-}$ 3.89 SEM with a range of between 5.6mls to 95.1mls and 55% of the patients having gastric volumes of above 25mls.

Patients who received I.M. metaclopramine 10mg in groupll showed a significant decrease in the mean gastric volume of 10.23$^{+}_{-}$ 1.59 SEM as compared to 37.5mls $^{+}_{-}$ 3.89mls SEM of group 1 patients. Patients in group 11 had gastric volumes ranging between 1.8ml and 45.2ml and 22.5% of the patients has gastric volumes of above 25mls.

Patients who received Ranitidine 50mg in group 111 showed an even better result than groups 1 and 11 in that they had an even lower mean for gastric volumes of as low as 9.08±1.20mls SEM and gastric volume ranging between 2.0ml and 28.9ml and only 12.5% of the patients had a gastric volume of above 25mls with 75% of the patients having gastric volumes of below 10.0ml.

The combination of Metaclopramide with Ranitidine in group 1V did not show particular advantage over patients from groups 111 + 11 as far as gastric volumes are concerned. The mean gastric volumes for groups 1V were 9.72mls± 1.3mls SEM with gastric volumes ranging from 2.0mls to 30.0mls and 15% of the patients having a gastric volume of above 25mls.

Table 8 shows us the frequencies of potential risk in each group taking pH below 2.5 and the gastric volumes of above 25mls as the criteria of risk of pulmonary aspiration of gastric contents. As high as 30% of the patients in group 1 had a combination risk of both pH below 2.5 and gastric volumes above 25mls. Group 11 had about 12.5% of the patients falling under the same category,

while groups 111 and 1V had 0% patients each which shows that the risk of the patients in groups 111 and 1V of having acid aspiration pneumonitis is very low as compared to groups 1 and 11 and in particular group 1.

Assuming that the criteria of poor risk are a pH below 2.5 and a gastric volume of above 25mls, it was considered to put patients who were 'safe' from acid aspiration under a separate group as those patients having a pH of above 5.0 and a gastric volume of less than 25mls. This group has also been indicated in table 8. Group 1 having the lowest margin of safety as 2.5%, group 11 increasing the safety to 22.5% and group 111 having patients with both pH above 5.0 and gastric volume of below 25mls are as much as 75%. Group 1V however shows a 62.5% margin of safety.

In addition table 7 shows the variation of gastric volumes of less than 10mls in the 4 groups. Group 1 had 5% patients with gastric volumes of less than 10mls. Group 11 65%, group 111 75% and group 1V 80%. This high percentage in groups 11, 111 and 1V show the effectivity of Metoclopromide,

Ranitidine and their combination in reducing gastric volumes pre-operatively.

Further comparison between control patients in group 1 and in those who had been given Ranitidine preoperatively in group 111 is illustrated graphically in a scatter diagram in table 9 where the pH of gastric aspirates rises higher where more time is allowed from the time of injection of Ranitidine, peak values being obtained between 90 and 120 mins after injection. In contrast the control patients gastric pH changes very little if at all with time and that also, it has a tendency of having a pH lower still.

Table 10 shows the change of pH in the control group 1 with duration of starvation. As the patient is starved longer, the pH decreases further and further. This means that even the patient who is starved for more than 12 hrs for elective surgery may be of value only in reducing gastric volumes and allows stomach emptying overnight.

Table 11 illustrates anaesthetic technique versus approximate blood losses in the 4 different

groups. Blood losses were noted between 200mls and were put into 4 columns. 47 out of 160 patients had blood loss ranging between 600-799mls and another 69 patients out of 160 had blood losses ranging between 400-599mls. There were no patients who had a blood loss of above 1800mls in any group. The distribution of blood losses were evenly distributed and the study does not show any tendency of increased uterine bleeding in patient who were injected metoclopromide and ranitidine in coparission to the control group, using the same anaesthetic techniques in all four groups.

Table 12 shows the variations for the indication of surgery in each group. On the average 36% of the surgery is due to patients having previous caesarian scars in established labour. Another 20% on the average are operated due to obstructed prolonged labour due to Cephalo pelvic disproportion, while 17.5% of the paients are operated due to fetal distress due to different causes.

Distribution of Apgar scores (less than 6) of infants related to the type of pre-medication given is illustrated in table No. 13. It is evident that the percentages of low apgar scores are evenly distributed amongst the 4 groups without any predesposition of the infants in groups 11, 11 and 1V to any greater distress than in group 1.

Table No. 14 compares the number of patients who underwent surgery as emergencies to those as elective caesarian section. It can be noted that on the average only about 5% of all cases are elective and 95% emergencies. Distribution of patients according to ASA classification is shown in table No. 15 having about 89% of the patients in ASA 1 and about 11% in A.S.A. 2.

DISCUSSION.

Active vomiting may occur during light anaesthesia when the reflex is liable to be initiated by Laryngoscopy, intubation, intermittent positive pressure ventilation by mask, hypotension, hypoxia and other factors. It is most likely to occur during induction or at reversal when airway is not protected with an endotracheal tube and cuff. Closure of the clottis is part of the complex reflex act of vomiting. Therefore prompt evacuatiion of the pharynx by suitable posture and suction usually prevents aspiration and tracheobronchial soiling.

Regurgitation into the pharynx occurs when there are gastric contents lying in the oesophagus and the cricopharyngeal sphincter is relaxed by general anaesthesia, particularly when the relaxant drugs are used. The glottis is usually incapable of closure either because of neuromuscular blockade, with the relaxant drugs

or because of depression of protective reflex closure of surgical anaesthesia.

Aspiration of acid gastric contents into the lungs produces an inflammatory reaction with a cellular exudate and loss of bronchial epithilium. The oedema fluid may be haemorrhagic. There is leucocyte infiltration and paranchymal distruction. Alveoli are filled with hyline exudate and extravasated red cell.

Mendelson's (1) or acid aspiration syndrome is a serious condition which may follow the aspiration of gastric contents into the air passages. Mendelson (1946) described the clinical picture after acid aspiration as cyanosis, dysponea, tachycardia, bronchospasm and in fulminant cases either acute oedema of the lungs or active respiratory failure. The radiograph shows a regular mottling without atalectasis. An interval of some hours may separate the initial aspiration from the development of the symptoms most commonly seen in obstretic patients perhaps because of their acute deprivation of Adrenoconticotropic hormone and corticosteroids following seperation of the placenta.

Solid food in the air passage may cause death due to total obstruction or atelectasis due to partial obstruction. One or other of these events was reported by Mendelson (1) in 5 out of a series of 66 obstetric anaesthetic complicated by inhalation of vomitus. He reported the aspiration of liquid vomitus in 61 cases and in only 45 of these was the event noticed at the time of occurance. 61 patients developed asthma-like reaction with wheezing, rales and rhonchi, 55 developed cyanasis. All had a pulse rate over 110 per minute and respiratory rates over 30 per minute. Cardiac failure and pulmonary oedema occured frequently. In Mendelson's series chest pathology was bilatral in 23% and right sided in 77%. Probably due to the anatomical position of the right bronchus which is shorter (2.5cm) and more in line with the trachea than the left bronchus and is greater in diameter. Hence a foreign body passes more easily into it than the left bronchus. He produced a syndrome in animals, similar to the one above by instilling liquid vomitus and 0.1 N HCL into thein tracheas.

Death may occur from the complete obstruction of the air passage by large food aprticles, or the reaction produced by the acid gastric aspirate, the nature and amount of the latter determining the severity and extent of the resultant reaction (Wynne and Modelle 1977) (2).

Death from pulmonary acid aspiration syndrome is due to progressive hypoxia resulting from exudates in the alveoli causing a $\dot{V}/\dot{Q}$ mismatch and shunting of blood. This hypoxia may not be reversed inspite of intermittent high positive pressure ventilation with 100% O_2.

The incedence of morbidity and mortality due to aspiration of gastric acid contents is high especially in emergency and obstetric anaesthesia.

Mendelson's (1) study showed 2 deaths out of 66 patients who had aspirated out of a total of 44,016 anaesthetic cases studied. i.e. approximately one death out of 22,008 anaesthetics given.

In a computer aided study undertaken by G.N. Olsson et al (3) covering 185 , 358 anaesthetics during a period of 1967 to 1983 showed an average of one death out of 46,340 cases was directly associated with acid aspiration.

S.K. KAHUHO and AYIM E.N. (4) 1972 to 1979 carried out a study on the causes of deaths occuring within 24 hours of surgery under general anaesthesia and out of 88,518 anaesthetics administered. Out of these 301, 5 deaths were due to acid aspiration. The incedence of death associated with acid aspiration was approximately one death in 17,700 anaesthetics administered.

In a dessertation study carried out by OGOLA E.G. (5) 1986 in which 98,677 patients underwent general anaesthesia between 1979-1985 at Kenyatta National Hospital, 9 out of 330 deaths were due to acid aspiration. That is approximately one death in every 11,000 anaesthetics administered was due to aspiration of gastric acid contents.

Not all the patients who aspirate die, some have mild clinical respiratory distress, while others go into pulmonary oedema and are admitted in the intensive care unit for mechanical ventilation with positive end expiratory pressures. Not all incedences of acid aspiration are documented and hence it is difficult to assess the incidence of aspiration and of morbidity. G.L. OLSSON (3) showed the incidence of aspiration as 4.7 in 10,000 cases i.e. one in every 2,131 cases had aspirated. Mendelson (1) showed that 66 patients aspirated out of 44,016 cases. i.e. an incidence of aspiration of 1 in 667 cases. We do not know the exact incidence of acid aspiration in Kenyatta National Hospital as not all incidences are documented.

In 1952 Taebeaut (6) corraborated Mendelson's findings and described a critical pH of less than 2.5 required to produce pneumonitis in rabbits. Volumes of gastric juices as little as 25mls and gastric pH levels less than 2.5 will generally produce severe pulmonary damages (6). Experiments have been done on rats in the development of

aspiration pneumonitis. Experiments (8) (Exarhos N.D. et al) have also been done on isolated canine pulmonary lobe models by instilling gastric acid aspirates, 0.1 N HCL and neutralized gastric acid aspitates into the brochus of these pulmonary lobe models. Weight changes due to intrapulmonary shunting was noted in each group and comparison was made between the weight changes in instilling neutralized gastric aspirates and even neutral distilled water. It was seen that there was most significant weight gain and hence pumonary shunting when pH was low especially below 2.5

It is agreed in general that a pH of less than 2.5 is the critical level for producing the aspiration pneumonitis syndrome.

Roberts and Shirley (9) suggested that pulmonary aspiration should be considered as a threat to pregant patients if they have greater than 25 mls of stomach contents. Larger volumes of acidic aspirates have been shown to produce greater morbidity and mortality in animals (8-9).

The prophylactic use of antacids before surgery seems to be a logical method of combating Mendelson's syndrome (10). The efficiency of antacids has however been questioned (11) and pulmonary aspiration of antacids alone, especially the particulate may itself lead to severe pulmonary damage (12).

Antacids:

Although they reduce the acidity, being liquids, they increase gastric volume-Hurwitz et al (13) have shown that using ^{51}Cr-sodium chromoglycate and a gamma camera that gastric emptying is prolonged significantly by aluminium hydroxide. Furthermore Feurle (14) has shown that apart from raising pH the use of a number of antacids was accompanied also by an increase in serum gastrin concentrations, which cause an acid rebound.

Mist Magnesium Trisilicate:

First used by Taylor et al (10) 1966 15 mls 2-hourly maintains a safe intragastric pH. Crawford 1971 (15) showed that 10 mls Magnisium Trisilicate given 10-15 mins before induction of anaesthesia-only 2% patients had a pH of less

than 2.5 at the end of caersarian section therefore duration of effectiveness is about 7 hours. Magnisium Trisilicate has a disadvantage of being particulate. Gibbs (12) et al 1979 showed that instillation of particulate antacid into the lungs of dogs produced an extensive reaction which persisted for at least one month, the focus being the antacid particulate itself.

Sodium Citrate

A non particulate antacid which mixes with gastric contents to a better extent than Magnisium Trisilicate, Lahari S. K. et al (16) 1973 were the first to use Sodium Citrate. They gave 15 mls of a 0.3mol solution to 22 obstetric patients 5-15 mins before induction of anaesthesia. This was effective in increasing the intragastric pH to greater than 3 in all patients for the duration of surgery.

Foulkes and Jenkins (1981) found that (17) larger doses of up to 30 mls of a 0.3 mollitre concentrations have been used, however this increases the mean intragastric volume to above 40 mls average. The duration of effectiveness for Sodium Citrate is 3 hours at a dose of 15 ml 0.3 mol concentration given 10 mins before induction, in elective patient

undergoing non-gastric surgery. The advantages of a smaller dose are a reduction in the total volume of stomach contents and a reduction in the frequency of side effects, including nausea and diarrhea

However White & Clarke et al (18) observed that Sodium Citrate was ineffective and that 19% of patients given 15 mls of Sodium Citrate 0.3 mol litre just before induction of anaesthesia had gastric contents with a pH less than 3.

More recently Radio measurements by O'Sullivan et al 1983 (19) have observed that one of the principal determinants of the duration of action of antacids is the rate of gastric emptying, and that any factor which delays this (for example narcotic analgesics or general anaesthetics) would prolong the effect of the antacid.

OTHER ANTACIDS

Taylor (1966) (10) found that colloidal aluminium hydrochloride failed to increase the pH of the stomach contents above 2.5 in 12.5% of patients. Using Gelusil, a mixture of magnisium trisilicate and aluminium hydroxide, given approximately 60 mins before induction, Dewan and others (1982) (20)

reported that 35% of the patients had intragastric pH of less than 2.5. A single dose of milk of magnisia has also been reported as being effective in increasing the pH to more than 2.5, when given to obstetric patients 10-18 minutes before anaesthesia.

INHIBITION OF GASTRIC ACID PRODUCTION

Antiocholinergic Agents

Anticholinergic agents inhibit the vally mediated production of gastric juice thereby decreasing gastric secretion and increasing gastric pH but only to a highly variable degree. They also have side effects which include tachycardia, delayed gastric emptying and a reduction of the lower oesophageal sphincter tone thereby perhaps increasing the susceptibility to regurgitation and aspiration (21) Baraka and Associates (22), in studying the effects of glycopyrrate before caesarean section, found that gastric pH was greater than 2.5 in 66% of cases following glycopyrrolate, whereas atropine had not significant effect on gastric pH. Salem and others (23) found that in 58.1% of children premedicated with glycopyrrolate, gastric pH was greater than 2.5. The above results are promising but in a recent study by Stoelting R. K. (24)

glycopyrolate failed to change significantly either pH or volume of gastric contents compared with values in control patients.

As anticholinergic agents only inhibit vagally mediated gastric acid production, it is not surprising that effects on intragastric pH are variable and largely ineffective. These drugs therefore are unsuitable for use alone in the prevention of acid aspiration. Dewan et al (25) showed that the combination of anticholinergic agents with antacids are much more effective in reducing gastric acidity.

Histamine has a major role in hydrochloric acid production by parietal cells in the stomach, an effect mediated by histamine-2 (H_2) receptors. The discovery and introduction of H_2-receptor blocking drugs has provided a new therapeutic approach to the treatment of gastric hypersecretory states.

ASH and Schild (26) postulated the existence of more than one type of histamine receptor. Histamine H_1 receptors are present in arterial, intestinal and bronchial smooth muscles. These H_1 receptors are antagonized by the classic antihistamines. The other actions of histamine are the stimulation of the heart muscle and the stimulation of gastric secretion.

These effects are blocked by histamine H_2 receptor antagnosists e.g. cimetidine and Ranitidine.

Histamine is composed of an imidazole ring. H_1-receptor antagonists have a modified ring or no ring at all, whereas H_2 receptor antagonists retain the ring and have modified side chains. Black et al in 1972 synthesized the first H_2-receptor antagonist, burimamide, which proved to be effective in reducing histamine stimulated acid secretion in animals and man. Because burimamide is not readily absorbed from the gut, another H_2-receptor antagonist, Metiamide, structurally similar to histamine and more potent in reducing acid secretion was synthetized. However several cases of agranulocytosis were reported with the use of metiamide and it was attributed to the thiourea group in metiamide. Replacement of the thiourea group in metiamide with cyanoguanidine resulted in the H_2-receptor antagonist cimetidine which has proved to be clinically effective and soon become popular. As cimetidine has a number of untowad effects associated with its use, continuing research led to the development of several new agent like Ranitidine, Tiotidine, Ormetidine, SKF 93474 and etinidine. Some of these compounds are still undergoing clinical trials.

Cimetidine

Cimetidine is a weak imidazole base and peak blood levels are achieved 45 to 60 mins after oral administration. The plasma half-life is approximately 2 hours in subjects with normal renal function. Although parentral administration of cimetidine achieves a higher peak drug level than that obtained by oral administration, clinically effective drug levels of 0.5 mg/ml are maintained for an identical period of four hours by either route. Cimetidine is excreted via the kidneys within 24 hours after oral or parentral administration, 48% to 77% of the drug being excreted unchanged. The rest of the cimetidine is excreted in the form of metabolites. The sulfoxide is the major metabolite. Sulfoxide is a product of hepatic inactivation by conversion of the side chain thioether.

Cimetidine is a reversible, competitive H_2-receptor antagonist. In man three endogenous acid secretogogues are histamine, gastrin and acetycholine. Cimetidine inhibits gastric acid secretion produced by all conversional stimuli. This if interpreted is an evidence that histamine is part of the final common pathway to parietal cell activation (27).

Cimetidine inhibits basal and noctural gastric acid secretion and acid secretion stimulated by histamine, pentagastrin, caffeine, insulin and food. The inhibitory effect of oral cimetidine on gastric secretion begins 60 to 90 minutes after administration and reaches it peak at 120 to 150 minutes. At plasma concentrations of 0.5 mg/ml, basal secretions was suppressed by more than 80% and secretion stimulated by food and gastrin was suppressed by more than 50% (28) when administered in four doses totaling 0.8 to 1.6 g, cimetidine suppresses 24-hour intragastric acidity both in normal subjects and patients with deudenal ulcers by 70% (29). The inhibitory effect of cimetidine on stimulated gastric output includes a marked decrease in both hydrogen ion concentration and gastric juice volume. Pepsin output generally decreases in parallel with the diminished volume of gastric secretion. Fasting serum levels of gastrin are uneffected by cimetidine. Cimetidine has no consistent effect on the rate of gastric emptying, lower oesophageal sphincter pressure or on the pancreatic secretion.

Side effects and toxicity of cimetidine during short term therapy include headaches, dizziness, fatigue, muscle pain, fever, constipation or diarrhoea, skin rash. Reversable elevation of serum transaminase have

been noted, rarely elevation in alkaline phosphatase levels have also been noted. Biopsy of the liver has proven periportal hepatic necrosis and centrilobular necrosis in two patients - Ganycomastia in men and galactorrhea in women. Reversable inhibition of tubular secretion causes a high creatinine level. There have been infrequent reports of agitation mental confusion and even coma with high doses (serum, cimetidine levels above 1.25 mg/ml), with improvement on cessation of the drug.Mogelenicki and colleagues reported arousal following physiostigmine in two such cases. Bradycardia, hypotension, cardiac arrythmias and even cardiac arrest have been reported following intravenous cimetidine. Heamatological abnormalities and bone marrow suppression include granulocytopenia, leukopenia, agranulocytosis and thromocytopenia. Inhibition of drug metabolism by cimetidine is an important drug interaction. Cimetidine inhibits microsomal drug metabolism in the liver, this action is perhaps due to binding to microsomal P-450. As a result the half life of antipyrine is increased due to decreased clearance. Similarly, the metabolism or anticoagulants, barbiturates, benzodiazepines, propranalol and theophylline is decreased and the duration of action increased by cimetidine. Cimetidine prolongs prothrombin time in patient given oral anticoagulants.

Cimetidine decreases liver blood flow, hence cimetidine may interfere with the clearance of lignocaine as the lignocaine clearance is dependant on hepatic blood flow.

The efficacy of preanaesthetic cimetidine in reducing gastric pH and volume is variable depending on the dose and route of intake and it is used commonly with an antacid or an anticholinergic agent.

A single dose of 300 mg cimetidine orally 60 to 120 minutes before induction of anaesthesia was compared with anticholinergic and antacid premedication and was demonstrated to be significantly more effective. Husemeyer et al (30) showed that 60% to 80% of elective surgical patients arrived in the operation room with gastric pH levels less than 2.5. In contrast one dose of 300 mg cimetidine administered in the morning or the night before surgery increased the gastric pH to greater than 2.5 in 70% to 100% of patients.

A single dose (intravenous) regimen has been shown to be superior to oral administration (31), as higher peak plasma levels are achieved during the first hour and a decline in gastric volume within

15 to 60 minutes. When given 45 minutes before anaesthesia the gastric pH increased to greater than 2.5 in 90% patients. The mean gastric pH was 1.73 $\pm$ 0.07 before administration of cimetidine and increased to 4.43 $\pm$ 0.15 after two hours. Total acid concentration was reduced to 98% after cimetidine.

Patients having emergency surgery pose high risk of pulmonary aspiration. Dobb and associates (32) studied the effect of 200 mg of cimetidine administered intravenously to 20 patients scheduled for emergency surgery and expected to have full stomachs. The gastric pH was evaluated to greater than 2.5 in 80% of the patients 1 hour after cimetidine administration and was greater than 4.0 in all patients after induction of anaesthesia.

Dundee and associates (33) described their experience with cimetidine in obstetric anaesthesia in over 5,000 patients for pre-anaesthetic prophylaxis. Preliminary trials of intravenous and oral cimetidine were followed by a large field trial in which a 400 mg oral loading dose was given at establishment of labour followed by 200 mg every 2 hourly. In the patients who received 200 mg intravenously 60 to 80 minutes before induction, gastric pH was

greater than 2.5 in all. One third of patients had gastric pH less than 2.5 when the interval between administration of cimetidine and induction of anaesthesia was 30 to 40 minutes or more than 90 minutes. In the field trial only 4% of the patients had gastric pH less than 2.5 when cimetidine was administered.

Ranitidine is a substituted amino-alkylfuran derivative which markedly inhibits basal and noctural gastric acid secretion as well as secretion stimulated by histamine, pentagastrin, sham-feeding and meals. Ranitidine is rapidly absorbed after oral administration achieving peak plasma levels after 60 to 90 minutes, therapeucally effective plasma concentrations last at least 8 hours which outlasts that of cimetidine. Most of the drug is excreted in the urine unchanged with an elimination half life of approximately 2 hours. On the Molar basis, Ranitidine is 4 to 7 times more effective than cimetidine as an antisecretory agent. Damman and associates (34) have shown in two different studies that a single dose of 100 mg of oral ranitidine increases gastric pH to greater than 7.0 for 7 to 8 hours whereas a single dose of 150 mg orally suppresses basal acid output by 70% and pentagastrin stimulated secretion by 40% in healthy

volunteers. In addition, 150 mg of ranitidine administered orally three times daily produced gastric pH values of 7.0 for 24 hours in patients undergoing parentral nutrition with previous intragastric pH levels of 2.0 or less. There are no obvious side-effects that would preclude the use of Ranitidine in man. Ranitidine does not inhibit drug metabolism by microsomal enzyme systems.

The last meal bears little relationship with the volume of gastric contents at induction of anaesthesia. A fast of four hours is no guarantee of an empty stomach, even before elective surgery in prepared patients significant gastric volumes may be present. In addition to recent ingestion of food, there are a number of factors which delay gastric emptying-including emotional states, pain toxicity and the use of narcotic agents (Nimmo et al 1978)(35) Attempts may be made to empty the stomach before operation either by mechanical or pharmacological means.

Passage of a nasogastric tube is inadequate for emptying the stomach before anaesthesia. A wide bore oesophageal tube should be used. The tube should be moved into different positions and the stomach should also be aspirated with the patient on the left side.

Apomorphine - a morphine derivative which is a powerful stimulator of the chemoreceptor trigger zone is commonly used as an emetic. However it should be used with caution as it causes cardio-vascular collapse.

Metoclopramide is a dopamine antagonist structurally related to procainamide. It causes intensified gastric parystalsis and dilatation of the pylorus, leading to gastric emptying. Metoclopramide also increases the tone of the lower oesophageal sphincter and increases the barrier pressure thereby reducing the risk of regurgitation into the oesophagus. Howells and Colleagues (36) showed that metoclopramide 20 mg orally was effective in emptying stomachs challenged by a water load. They also used barium swallow radiography in trauma patients requiring general anaesthesia If stomach residues present I.V. metoclopramide 20 mg resulted in emptying of the stomach in 30 minutes if a 'light' meal had been taken, but in 90 minutes following a 'heavier' meal. In patients in labour, they found that the volume of 750ml test meal of water was reduced significantly more rapidly when patients were given metoclopramide 10 mg I.M. Although metoclopramide does appear to be effective in reducing intragastric volume its effects are completely abolished by narcotic

analgesics Nimmo (37) or by a preceding injection of anticholinergics especially atropine, which alters the tone of the lower oesophageal sphincter.

Accurate gastric emptying may be assessed by following the removal of radioactive material from the stomach, or by administration of large volumes of fluid containing indicator dye. Clements and colleagues (37) have shown that the absorption of orally administered paracetamol correlates well with gastric emptying as determined by serial scintiscans of the abdomen. Apart from the lightness of anaesthesia and other factors concerned with vomitting as mentioned above two very important factors which effect regurgiation are the rate of gastric emptying and the tone of the lower oesophageal sphincter.

Factors delaying gastric emptying are recent ingestion of food, emotional state, pain, presence of large abdominal tumours and masses, pregnancy, obesity, chronic diseases and cachexia, chronic toxicity due to infections and the use of narcotic analgesics. Nimmo (35).

The lower oesophageal sphincter was first demonstrated by FYKE in 1956 as the existence of a high pressure zone at the lower end of the

oesophagus. It is the major barrier preventing the regurgitation of acid gastric contents into the oesophagus and hence the pharynx (38). In man the lower oesophageal sphincter is 2 to 5 cm long and extends both above and below the diaphram and it maintains a resting pressure greater than that of gastric. The resting zone of the lower oesophageal sphincter is an intrisic property of the muscle layers in that region. Some other anatomical features that help the lower oesophageal sphincter in its function are the angle at which the oesophagus meets with the fundus of the stomach acting as a flap value. The intra-abdominal length of the oesophagus may act as a flutter value and the diaphragmatic crurae may act as a pinchcock on the lower oesophagus. The sphincter relaxes on swallowing to allow the passage of food into the stomach. The tone of the sphincter increases proportionally as the intragrastic pressures rise to well above the intragastric pressures. Although the tone of the lower oesophageal sphincter is an intrisic property of the musculature, it may be altered by a large variety of neural, hormonal and drug influences.

Factors increasing the lower oesophageal sphincter tone are: metoclopramide, histamine, suxamethonium, pancuronium, antacids and others.

Factors that decrease the lower oesophageal sphincter tone include atropine, glycopyrolate, dopamine, opiates, thiopentone, halothane, enflurane and others.

Drugs that have no effect on the lower oesophageal sphincter tone include propranalol, cimetidine, ranitidine, atracurium and possibly nitrous oxide.

During pregnancy the increased intra-abdominal pressures as a result of intrauterine enlargement, the lower oesophageal becomes paradoxically incompetent and patients commonly complain of heartburns and refluxes due to regurgitation.

Van Theil and Wald showed in 1981 that the lower oesophageal sphincter pressure is lowest at 36 weeks of pregnancy possibly due to changes in the progesterone:oestrogen levels.

It is advisable to avoid hypoxia by preoxygenating the patients for at least 3-4 minutes before induction, avoid hypotension by putting the patient in the left lateral position or a 15 degree tilt of the table to avoid the uterine compression of the aorta and the vena cava. Hypotension can also be avoided by using smaller doses of thiopentone at induction.

Failure of manoeuvers e.g. Sellicks procedure, (cricoid pressure) can allow a silent regurgitation of gastric contents. After having induced the patient do not give 100% O_2 by intermittent positive pressure ventilation with bag and mask. This irritates the stomach by distension and retching occurs followed by active vomiting. Inability to intubate the trachea often causes panic and prolongs hypoxia in failed intubations especially in junior staff who then apply vigorous intermittent positive pressure ventilation by mask and repeated laryngoscopy in a desparate attempt to intubate. A failed intubation drill by Tunstall (39) should therefore be used and no more time wasted in attempting intubation.

Inflation of the cuff is essential and despite an adequately inflated cuff, regurgitation has been reported by use of dyes. It is also important for the anaesthetist to check his equipment well before induction, having a working laryngoscope, introducer, different sizes of tubes, Magill's forceps, working suction machine and catheters, prepared drugs and competent assistant.

This study was done on 160 patients all falling in ASA group 1 and 11, having a mean age of about 24 years and mean height of 5.2" with a mean weight of 64.6 kg. The patients were divided into 4 groups (Table 1). The basal (control group patients) pH was found to be as low as 3.19 ± 0.21 SEM with a range between 1.8 and 6.8, 57.5% of the patients having a pH of less than 2.5 This data shows that the patients coming for emergency surgery in the maternity theatre Kenyatta National Hospital run an extremely high risk of acid aspiration and its complication. Due to the rapid turnover of patients and the sudden decisions made to go in for surgery, it was thought best to use our agents parenterally. Intramuscular Metoclopromide 10 mg and/or I.M. Ranitidine 50 mg at least 30 minutes prior to surgery.

This study was undertaken to enable us to find out the mean pH values and gastric volumes of our contingent of patients at the Kenyatta National Hospital, and also to accordingly study and suggest possible ways of combating acid aspiration syndrome in our set up. The difficulties however being the same as in any other developing country. Patients have a tendency of delaying admission into labour ward until they are in established

labour, inability of some patients to attend antenatal clinics, problem of transportation from long distances. Most of the elective patients from the wards eventually become emergencies as they wait too long in the wards due to lack of blood or due to lack of operation theatre as there is always an emergency which bypasses these elective cases. The ratio of elective to emergency ceasarian sections in Kenyatta National Hospital maternity theatre was found to be 1:20 i.e. 5% with an output of between 6 to 10 ceasarina sections every 24 hours.

It is evident that after injecting Metoclopromide in patients in group 11 the mean pH did not raise significantly to bring the patients out of the risk of acid aspiration. 45% of the patients still had a pH of below 2.5. But Metoclopramide definitely reduced the volume of gastric contents to a mean of 10.23 $\pm$ 1.59 S.E.M. and having as high as 65% of the patients with gastric volumes below 10 mls. (Table 7).

Following injections of Ranitidine in group III patients, the pH values rose to a mean of 6.03 $\pm$ 0.20 S.E.M. and 87.5% of the patients had a pH above 5.0, only one patient i.e. 2.5% had a pH of less

than 2.5. This however shows that although Ranitidine is effective, it is still not full proof and some percentage of patients will have a high risk of aspirating acid gastric contents. Ranitidine blocks the production of H+ by parietal cells but does not neutralize the already existing acid in the stomach. Ranitidine is seen to reduce the mean volume of gastric aspirates as effectively as Metoclopromide. This is due to its ability to increase gastric mobility and evacuation. The combination of Ranitidine and Metoclopromide in group IV (Table 8) shows that none of the patients in this group had a combination of pH less than 2.5 and gastric volumes above 25 mls. This is surely assuring and comforting and upto 62.5% of the patients had a pH above 5.0 and gastric volumes below 10 mls combined.

In a study done by G.B. Gillett et al (40) where single and multiple doses of 0.3M sodium citrate alone failed to elevate the intragastric pH above 3.0, led them to combine the antacid with oral Ranitidine. All 99 patients who were given this combination had a pH above 3.0. This shows that in this study it would have been even safer and more efficient to have given a single dose of a none particulate antacid 15 mls, 0.3M sodium citrate to all patients.

Another study by R. N. Francis and Kwik (41) showed the efficacy of a single dose of oral Ranitidine 150 mg given the night before the elective surgery. The incidence of gastric residue pH higher than 2.5 (p 0.01) was significantly greater in patients given Ranitidine than the untreated control group patients. The mean volumes of gastric aspirates in the Ranitidine group was 6.7 mls (Ranging between 2 to 20 mls) compared to the control group 15.6 ml (ranging between 2 to 44 mls).

L. Manchicanti et al (42) undertook a study using both Ranitidine and Metoclopramide for the prophylaxis of aspiration. Using the same critical factors above (6.7). She also compared the efficacy of Ranitidine over cimetidine in her previous study on cimetidine and metoclopramide (43). Manchikanti's works showed that 73% of control patients had a pH less than 2.5 and upto 47% of them had a gastric volume of above 25 ml. Metoclopramide and Ranitidine independently and in combination significantly reduce risk factors. Metoclopramide had a modest but significant effect on gastric volume and pH by reducing both the proportions of patients with either pH below 2.5 or gastric volume above 20 mls to 27%. Ranitidine with or without Metoclopramide by single or miltiple doses strikingly reduces gastric acidity and volume showing only 0.8% of patients

having a combination of large volume (above 20 mls) and acid gastric contents.

Ranitidine is a highly selective H_2 receptor antagonist with furan ring found in cimetidine. Ranitidine is rapidly absorbed, achieving peak plasmal levels in 60 - 90 minutes when taken orally with therapeutically effective concentrations lasting for at least 8 hours.

Damman et al (44) have shown that a single dose of 100 mg of Ranitidine increases gastric pH to greater than 7.0 for 7 to 8 hours which is of great importance to cover pre-operative, intra-operative and post-operative periods. Brater et al (45) demonstrated 86 and 98% inhibition of acid secretion after 150 and 300 mg of oral ranitidine respectively. It has also been shown that the effects of 150 and 300 mg of ranitidine last 10 - 12 hours after administration with 44 and 61% inhibition of acid secretion and mean intragastric pH values of 3.7 and 4.8 respectively at the end of the 10 hour period.

Ranitidine is also devoid of side effects that are seen within cimetidine. It does not cause hepatic and renal complications. There have been no report

of agitation, confusion and coma. No haematological abnormalities have been noted. Ranitidine does not bind with the microsomal P-450 and thus does not inhibit microsomal drug metabolism and protein binding. Its effect on the foetus has not yet been studied. But in our 160 patients the Apgar scores in the 4 groups did not vary significantly. Neither were there any significant increases in blood losses and haemodynamic changes both pre-operatively and intraoperatively.

It should be emphasised once again that the key to the problem of acid aspiration is prophylaxis and early detection of a silent regurgitation. Prophylaxis by reduction of pH either by use of anatacids or H_2 receptor blocking agents, reduction of gastric volume by use of drugs like metoclopramide on physical nasogastric suction or even induction of vomitting in the awake patient. If aspiration does occur, proper management of these patients will determine the mortality rate which is often as high as 50% to 70%.

Recommended measures of treatment of acid aspiration are:-

- Active suction of pharynx and removal of all solid particles endoscopy to remove any solid particles.
- Tracheal suction but not levage

- Avoid hypotension, hypoxia and rectify acidosis.
- Intermittent positive pressure ventilation with positive end expiratory pressure.
- Limited parentral fluids to avoid pulmonary oedema.
- Use of corticosteroids is still questionable.
- Antiobiotic coverage to avoid secondary infections.

CONCLUSION AND SUGGESTIONS:

From this study it has been concluded that the morbidity and mortality due to acid aspiration is high especially in obstetric practice, the cause being aspiration of acid gastric contents of pH below 2.5 and volumes of above 25mls. Prophylaxis is the most important weapon and several methods have been suggested. In this study the combination of I.M. Ranitidine 50mg and I.M. Metoclopramide 10mg was efficient enough to raise pH above 2.5 in 96% of the patients and to reduce the gastric volumes to below 25mls in 85% of the patients. This is an impressive result, but it is necessary to note that 15% of the patients still had a volume of above 25mls and 5% still had a pH of less than 2.5 although none of the patients had a combination of both high volumes above 25.0 and a low pH below 2.5. Ranitidine alone however showed better results as 97.5% of the patients had a pH above 2.5 and 87.5% of the patients had gastric volumes below 25mls.

As this study was carried out on assessing the risk of aspiration in obstetric patients who were undergoing emergency caesarian sections and often there is little time to prepare a patient preoperatively it is evident that these patients

in most cases would have had a recent ingestion of a meal have a gastric acid pH of about 3.19$^{+}_{-}$ 0.21 S.E.M. and a gastric volume of about 37.5$^{+}_{-}$ 3.89mls E.S.M. (valves from control group 1).

Injecting Ranitidine and/or metaclopramide may not help to decrease the risks of acid aspiration if the patients were to be induced in less than 15-20 min after premedication, because Ranitidine does not neutralize the already existing acid gastric contents and both drugs may not have enough time to work effectively in such a short time. An ideal time for induction is basically 60 to 90 min after the injection of Ranitidine (see table No.9) and metoclopramide. Therefore the patients who benefit from this study most are those patients with relative emergencies like prolonged labour due to cephalo pelvic disproportions but cases like cord prolapse who are anaesthetised as an acute emergency may not even give us enough time to even to premedicate them.

I therefore suggested that the battle of prophylaxis against acid aspiration syndrome should start at the establishment of labour/or at admission of into labour ward and not when the decision is

made to go into theatre. All patients admitted in labour should be given the following.

1. Oral ranitidine 150mg on admission, and then 150mg every 6 hourly plus another 150mg 2hours prior to surgery.

2. 15mls of 0.3m solution of sodium citrate at admissiion, and then 15mls every two hourly. This would neutralize the acid present in the stomach and another 15mls prior to induction if it is an emergency.

3. Patients admitted to labour ward who are in labour should not be given meals. Instead I.V. fluid would be of choice for fluid and electrolyte balance. This will help in reducing gastric volumes and avoid hypotension due to hypovolaemia.

4. Passage of an Nasogastric tube and 2 hourly suction in the very ill patients.

5. I.M. Metoclopramide 10mg at least half an hour or more prior to induction.

Avoid giving narcotic analgesics as this causes a delay in gastric emptying and reduces the tone of the lower oesophageal sphineter it also depresses the respiration of both the mother and the neonate.

6. When giving an injection of metoclopramide as premedication, avoid premedication with an anticholinergic e.g. I.M. Atropine 0.6mg as this will alter the efficacy of metoclopramide by altering the tone of the lower oesophageal sphincter. Atropine 0.6mg given intravenously at preoxygenation.

7. Position the patient in the left latral position or tilt the patient 15° with a wedge to avoid compression of the vena cava and abdominal aorta to avoid a reduction in venous return and reduction in cardiac output.

8. Induction and intubation with a head up position to avoid regurgitation due to gravity and have a powerfull working suction machine at hand.

9. Cricoid pressure and application of cuff to endotracheal tubes at induction.

10. In case of a failed intubation, employ a failed intubation drill.

11. A constant well instructed anaesthetic nurse for maternity theatre.

12. A good post-operative recovery room, with oxygen and suction available.

For patients who come in as acute emergencies I would suggest the following.

1. I.M. Ranitidine 50mg.
2. I.M. metoclopnamide 10mg.
3. Oral sodium citrate 0.3M 15mls.
4. N.G. tube suction and evacuation followed by the same techniques described above.

For patients who are undergoing elective surgery I would suggest the following:-

1. Tab Ranitidine 150mg the night before surgery.

2. Tab metoclopnamide 10mg the night before operation.

3. Tab Ranitidine 150mg the morning of surgery.

4. I.M. Metaclopnamide one hour before surgery.(10mg).

5. I.V. Atropine 0.6mg at induction.

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TABLE NO. I

ANAESTHETIC TECHNIQUE

GROUP	PREMEDICATION	PREINDUCTION	INDUCTION	PRE DELIVERY MAINTAINANCE	POST DELIVERY MAINTAINANCE	REVERSAL
I	NIL	I.V. Atropine 0.6mg 3-5 min prior to induction preoxygenation 5 mins	Cricoid pressure thiopental 250mg Suxamethonium 100mg	I.V. Pancuronium 4-6mg/dtc 30-45mg $N_2O:O_2$ 50:50% Closed circuit anaesthesia	I.V. ergometrin 0.5mg/oxytocin I.V. Pethidine 15mg $N_2O:O_2$ 66.33%	Atropine 1.2mg followed by neostigmine 2.5mg both I.V.
II	I.M. Metoclopromide 10mg half hour or more pre-operation	"	"	"	"	"
III	I.M. Ranitidine 50mg half hour or more preoperatively	"	"	"	"	"
IV	I.M. Metoclopramide 10 mg plus I.M. Ranitidine 50mg half hour or more Preoperatively	"	"	"	"	"

T A B L E N O. 2

PATIENTS DEMOGRAPHIC CHARACTERISTICS

GROUP	NUMBER OF PATIENTS	MEAN AGE (YEARS)	MEAN HEIGHT (FEET + INCHES)	MEAN WEIGHT (KG)
1	40	24	5'2"	66
11	40	24.5	5'2"	63
111	40	23	5'3"	66
IV	40	25	5'3"	63
TOTAL	160	24.1	5'2.5"	64.5

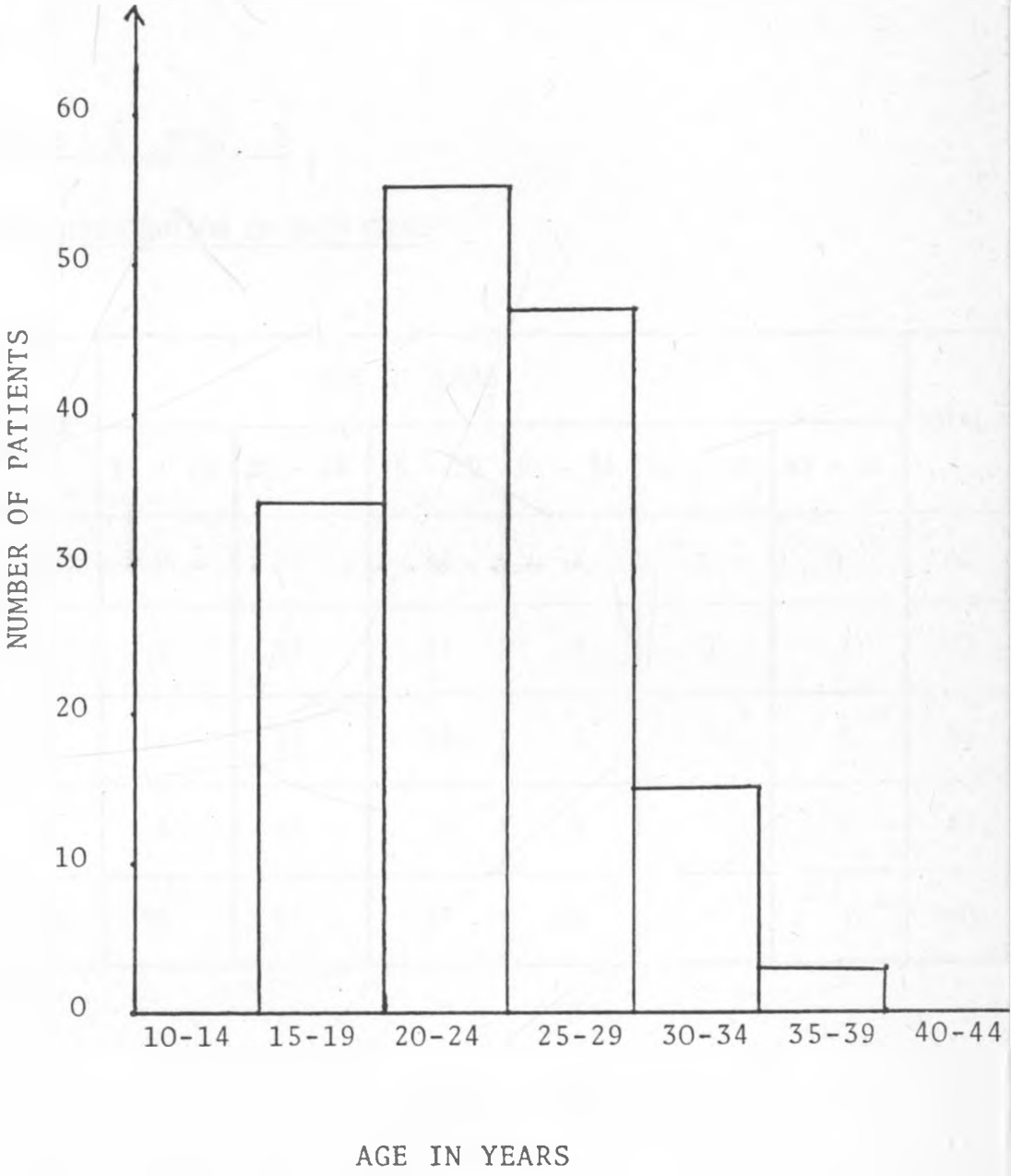
T A B L E N O. 3

AGE DISTRIBUTION

AGE IN YEARS	NO. OF PATIENTS	PERCENTAGE
BELOW 10	0	0
10 to 14	0	0
15 to 19	35	21.875
20 to 24	57	35.625
25 to 29	49	30.625
30 to 34	14	8.750
35 to 39	4	2.5
40 to 44	1	0.625
Above 45	0	0
TOTAL	160	100.0

T A B L E N O. 4

HISTOGRAM OF AGE DISTRIBUTION



T A B L E N O. 4

HISTOGRAM OF AGE DISTRIBUTION

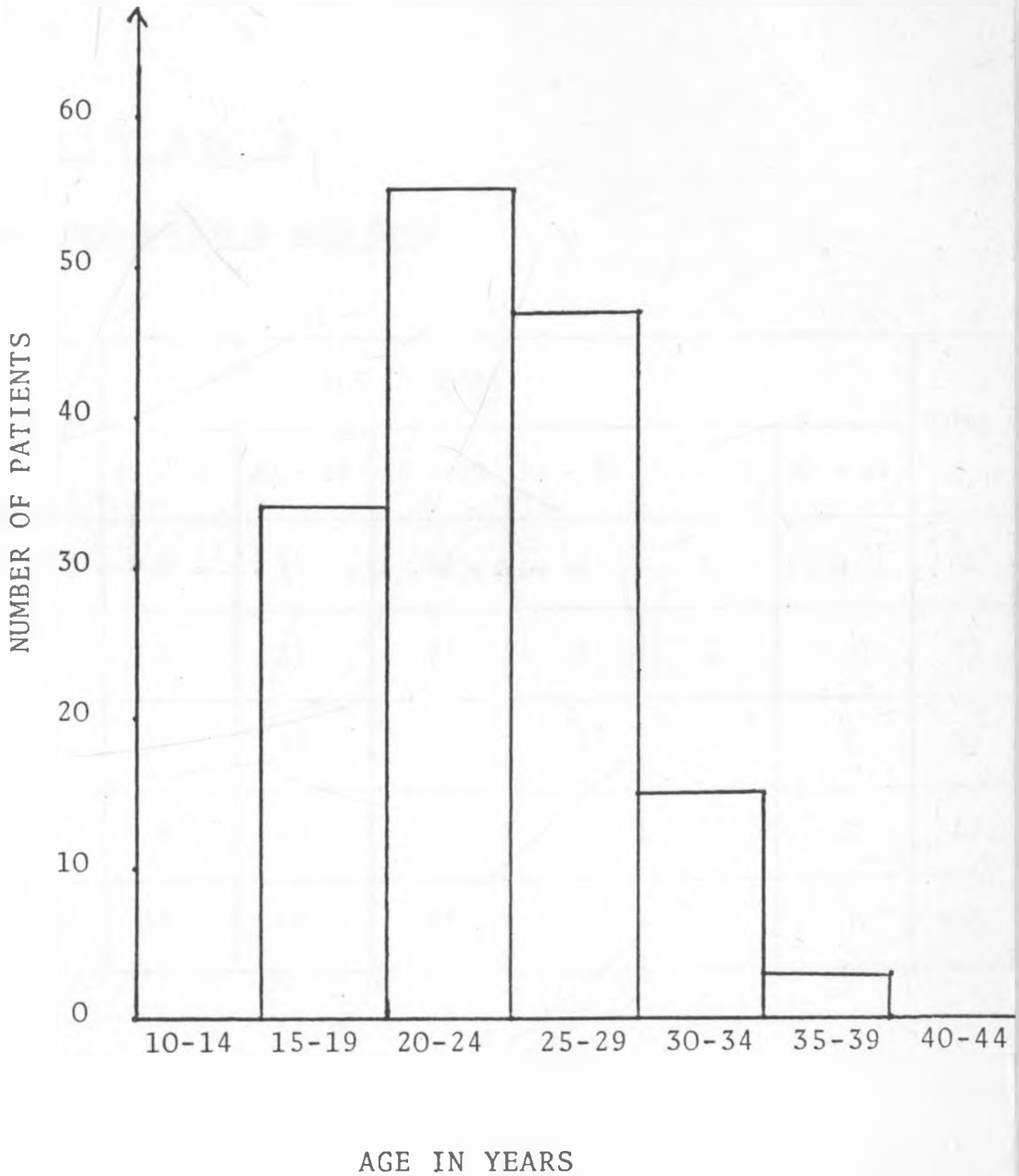


TABLE NO. 5

AGE DISTRIBUTION IN EACH GROUP

GROUP	AGE IN YEARS						TOTAL
	15 - 19	20 - 24	25 - 29	30 - 34	35 - 39	40 - 44	
I	9	15	13	2	1	0	40
II	9	11	13	5	1	1	40
III	11	13	14	2	0	0	40
IV	6	18	9	5	2	0	40
TOTAL	35	57	49	14	4	1	160

T A B L E N O. 6

GASTRIC pH CHARACTERISTICS

GROUP	pH		PATIENTS WITH pH BELOW 2.5		PATIENTS WITH pH ABOVE 5.0	
	MEAN ± S.E.M.	RANGE	NO	%	NO	%
I	3.19 ±0.21	1.8 – 6.8	23	57.5	3	7.5
II	3.47 ± 0.27	1.8 - 7.8	18	45.0	12	30.0
III	6.03 ± 0.20	2.4 - 8.6	1	2.5	35	87.5
IV	5.73 ± 0.25	2.2 - 8.4	2	5.0	30	75.0

T A B L E N O. 7

CHARACTERISTICS OF GASTRIC ASPIRATE VOLUMES

GROUP	VOLUMES IN MLS		PATIENTS WITH VOLUMES LESS THAN 10 MLS		PATIENTS WITH VOLUMES MORE THAN 25 MLS.	
	MEAN ± S.E.M.	RANGE	NO	%	NO	%
I	37.5 ± 3.89	5.6 - 95.1	2	5.0	22	55.0
II	10.23 ± 1.59	1.8 - 45.2	26	65.0	9	22.5
III	9.08 ± 1.20	2.0 - 28.9	30	75.0	5	12.5
IV	9.72 ± 1.30	2.0 - 30.0	32	80.0	6	15.0

TABLE NO. 8

FREQUENCY OF PATIENT HAVING POTENTIAL RISK FACTORES IN EACH GROUP

GROUP	PATIENTS WITH SINGLE RISK FACTOR.	PATIENTS WITH SINGLE RISK FACTOR.	PATIENTS AT VERY HIGH RISK.	PATIENTS IN THE SAFETY ZONE
	pH BELOW 2.5	VOLUMES ABOVE 25 MLS.	pH BELOW 2.5, VOLUME ABOVE 25 MLS	pH ABOVE 2.5, VOLUME BELOW 10MLS
I	23 (57.5%)	22 (55%)	12 (30%)	1 (2.5%)
II	18 (45%)	8 (20%)	5 (12.5%)	9 (22.5%)
III	1 (2.5%)	5 (12.5%)	0 (0%)	30 (75%)
IV	2 (5%)	6 (15%)	0 (0%)	25 (62.5%)

TABLE NO. 9.

COMPARISON OF pH VALUES OF GROUP I WITH GROUP III IN RELATION TO THE DURATION OF TIME SPENT AFTER AN INJECTION OF RANITIDINE 50mg.

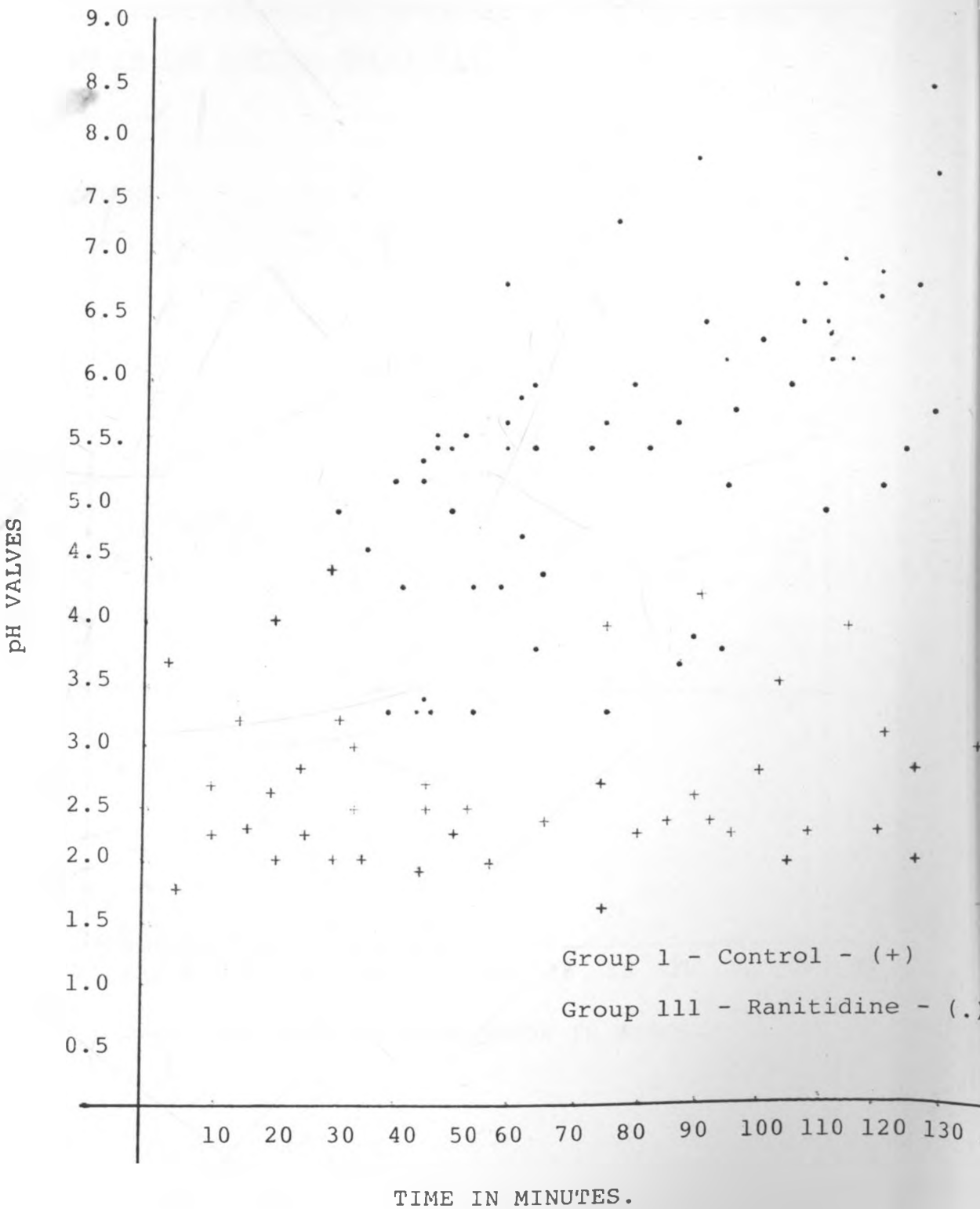


TABLE NO. 10

RELATION BETWEEN THE DURATION OF STARVATION AND THE pH IN THE CONTROL GROUP (I).

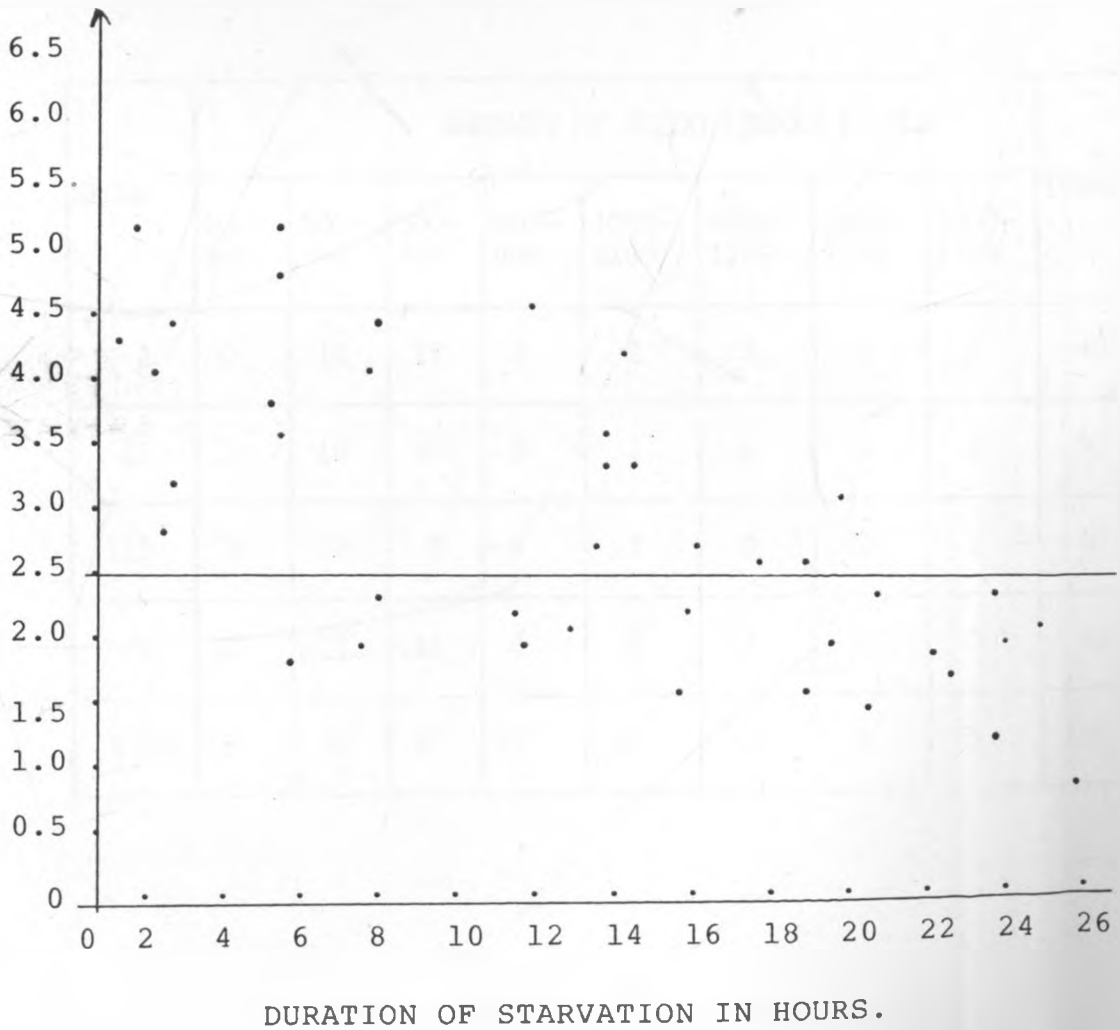


TABLE NO 11

ANAESTHETIC TECHNIQUE VERSUS APPROXIMATE BLOOD LOSS

GROUP	AMOUNTS OF BLOOD LOSSES IN MLS								TOTAL
	200-399	400-599	600-799	800-999	1000-1199	1200-1399	1400-1599	1600-1799	
I	0	14	17	3	2	1	1	2	40
II	1	19	10	5	2	0	1	2	40
III	2	18	9	5	3	0	2	1	40
IV	2	18	11	4	3	1	1	0	40
TOTAL	5	69	47	17	10	2	5	5	160

TABLE NO 12

VARIATIONS OF INDICATIONS FOR SURGERY

DIAGNOSIS	GROUP I	GROUP II	GROUP III	GROUP IV
OBSTRUCTED LABOUR DUE TO C.P.D.	25%	20%	17.5%	12.5%
BREECH PRESENTATION	2.5%	5%	2.5%	0%
SEVERE P.E.T.	5%	10%	7.5%	5%
TWIN PREGNANCIES	2.5%	2.5%	2.5%	5%
CORD PROLAPSE	0%	2.5%	2.5%	5%
PREVIOUS SCARS IN LABOUR	40%	35%	40%	32.5%
FETAL DISTRESS	17.5%	15%	15%	22.5%
A.P.H. DUE TO PLACENTA PRAEVIA	5%	7.5%	10%	12.5%
B.O.H. WITH REDUCED FETAL MOVEMENTS	2.5%	2.5%	2.5%	5%
TOTAL	100%	100%	100%	100%

T A B L E NO 13

DISTRIBUTION OF APGAR SCORES (LESS THAN 6) OF INFANTS RELATED TO TYPE OF PRE- MEDICATION

GROUP	I	II	III	IV
APGAR SCORE AT 1 MIN.	12.5%	10%	10%	7.5%
APGAR SCORE AT 5 MIN	2.5%	5%	2.5%	2.5%
APGAR SCORE AT 10 MIN	0%	0%	0%	2.5%

T A B L E NO 14

NUMBER OF PATIENTS UNDERGOING EMERGENCY IN RELATION TO ELECTIVE CAESERIAN SECTIONS

GROUP	EMERGENCY	ELECTIVE
I	38 (95%)	2 (5%)
II	38 (95%)	2 (5%)
III	37 (92.5%)	3 (7.5%)
IV	38 (95%)	2 (5%)

T A B L E N O. 15

A.S.A. CLASSFICATION

A.S.A.	1	2	3	4	5
GROUP I	35	5	0	0	0
GROUP II	36	4	0	0	0
GROUP III	37	3	0	0	0
GROUP IV	35	5	0	0	0
TOTAL	143	17	0	0	0

APPENDIX

CASE NUMBER .....

NAME .....

IP NUMBER .....

DIAGNOSIS .....

.....

HEIGHT ..... WEIGHT ..... AGE .....

PB ..... PULSE RATE .....

RESPIRATORY RATE ..... ELECTIVE/EMERGENCY...

.....

A.S.A.CLASSIFICATION .....

IS PATIENT SUFFERING FROM ANY GASTRIC LESION? .....

.....

DURATION OF STARVATION .....

TIME PREMEDICATION GIVEN .....

TIME OF INDUCTION .....

PREMEDICATION:	INDUCTION
I.M. METOCLOPRAMIDE .....mg	I.V. THIOPENTONE ..... mg
I.M. RANITIDINE .....mg	I.V. SUXAMETHONIUM ..... mg
TIME OF DELIVERY ..... MIN.	
TUBOCURARE .....mg	ERGOMETRIN/OXYTOCIN .....mg
PANCURONIUM ..... mg	PETHIDINE .....mg
TIME OF REVERSAL .... MIN.	
ATROPINE ..... mg	NEOSTIGMINE .....mg
DURATION OF OPERATION ..... MIN	

APPROX. BLOOD LOSS ..... mls .....

VOLUME OF GASTRIC CONTENTS ASPIRATED .....mls

pH OF GASTRIC ASPRIATE .....

APGAR SCORE OF INFANTS AT 1, 5 and 10 MINUTES .....

.....

NAUSIA AND VOMITTING AT REVERSAL ..... YES/NO

CLINICAL SIGNS OF REGURGITATION .....YES/NO

ANY RESPIRATORY DISTRESS NOTED .....YES/NO

POST OPERATIVE VISIT

DOES THE PATIENT COMPLAIN OF:-

CHEST PAINS ..... YES/NO

BREATHLESSNESS ..... YES/NO

COUGH ..... YES/NO

DID THE PATIENT DEVELOP:-

CYNANOSIS .....

TACHYCARDIA .....

FEVER .....

ANY SIGNIFICANT X-RAY CHANGES IF IT WAS DONE?....

.....

DID THE PATIENT ASPIRATE ACID GASTRIC CONTENTS AND

DEVELOP PNEUMONITIS OR PULMONARY OEDEMA? .....

.....

DID ANY PATIENT REQUIRE I.C.U. MANAGEMENT WITH I.P.P.V?

.....