An open-label antacid-controlled randomized trial on effectiveness of alginate-antacid preparation (Gaviscon®) in suppression of post-supper acid-pocket, night-time acid-reflux and symptoms in asymptomatic obese participants.

By

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LIST OF ABBREVIATIONS

BMI	Body Mass Index
GEJ	Gastro-esophageal junction [YYL1]
GERD	Gastroesophageal reflux disease
GERDQ	Gastroesophageal reflux disease questionnaire
GI	Gastro intestinal
H2RA	Histamine 2 antagonist
IV	Intravenous
LES	Lower esophageal spinchter
MMS	Medical Measurement System
MRI	Magnetic resonance imaging
MRS	Multiple rapid swallowing
NHMS	National Health and Morbidity Survey
NIDDM	Non insulin-dependent diabetes
PPI	Proton-pump inhibitor
SCJ	Squamocolumnar junction
TLESR	Transient LES relaxations
USM	Universiti Sains Malaysia

ABSTRACT[YYL2]

Gastroesophageal reflux disease [GERD] with symptoms of heartburn and acid regurgitation are a common disorder in Asian population especially in overweight and obese persons. Acid pocket in the proximal part of stomach after meals has been shown to be an important mechanism of GERD.The acid pocket is increasingly recognized as a source from which acid reflux events originate. The presence of this gastric acid pocket has become an attractive therapeutic target. Proton pump inhibitors have been shown to reduce acidity of the acid pocket however alginate antacid formulation is inconsistent effects have been reported. The alginate-antacid formulations are used for the symptomatic treatment of GERD and appear to act by a unique mechanism which differs from other groups traditional antacids.

METHODOLOGY

A randomized open-label study with antacid-control performed over 48 hours by continuous pH impedance and bravo capsule monitoring. Eighteen asymptomatic obese patients were separated into either alginate antacid group and non alginate antacid group [simple antacid] were studied for 48 hours using the ambulatory wireless capsule and pH impedance. Participants took either alginate antacid [Gaviscon Advance (GA), Reckitt Benckiser, UK] or non alginate antacid [Magnesium Trisilicate (MMT)] which had equivalent strengh of antacid after taken late night standardised meals.

OBJECTIVES

To determine post prandial suppression of the acid pocket, night time reflux and symptoms by an alginate antacid [Gaviscon Advance (GA), Reckitt Benckiser, UK] preparation compared with a non-alginate antacid preparation using ambulatory wireless capsule pH-metry and pH impedance in obese participants who took late night supper.

RESULTS

A significant difference in median pH at gastric cardia was seen with alginate antacid compared to non alginate antacid with a median difference of -2.67 (P value 0.008). Median number and duration of refluxes were also lower after alginate antacid vs. without antacid with a median difference of -2.21 (all P values < 0.05), however there were no changes in pH refluxate at 5 cm above lower esophageal sphincter (LES) .There were no differences in reflux parameters (number and duration of acid refluxes) with vs. without non alginate antacids (all P values > 0.05).

CONCLUSIONS

Compared to non-alginate antacid, alginate antacid formulation significantly suppresses acid pocket at the gastric cardia and reduces the number and duration of refluxate after late night supper although the pH at 5 cm above LES did not change.This is because the principal mechanism of alginate antacid is to displace and neutralise post-prandial acid pocket, rather than containing the reflux as previously reported.

ABSTRAK

Penyakit refluks gastroesophageal [GERD]dengan simptom pedih ulu hati dan refluks adalah penyakit biasa berlaku dalam kalangan penduduk Asia terutama dalam seseorang yang mempunyai berat badan berlebihan dan obese. "Acid pocket" yang terbentuk di bahagian perut atas selepas makan telah terbukti sebagai satu mekanisme penting dalam penyebab penyakit [GERD] ini."Acid pocket " juga telah dikenali sebagai punca dan sumber kepada berlakunya asid refluks tersebut dan ini menjadikan ia sebagai penemuan penting dalam pencarian ubat untuk mencegah penyakit ini. "Proton pump inhibitor" telah terbukti dapat menurunkan acid dalam perut akan tetapi alginate-antiasid formula menunjukkan kesan yang tidak konsisten dalam penurunan asid telah dilaporkan. Alginate-antiasid formula telah digunakan dalam rawatan penyakit refluks dan ia bertindak berbeza dalam mekanisme penurunan asid berbanding dengan ubat anti asid yang lain.

METODOLOGI

Satu kajian rawak, label terbuka dengan anti-asid-kawalan yang dilakukan dalam tempoh 48 jam dengan menggunakan pH impedans berterusan dan kapsul bravo. 18 pesakit obes dipilih secara rawak dan dibahagi kepada 2 kumpulan iaitu kumpulan anti-asid yang mengandungi alginate dan kumpulan anti-asid yang tidak mengandungi alginate. Kajian ini dilakukan selama 48 jam menggunakan kapsul tanpa wayar dan pH impedans catheter .Pesakit megikut kumpulan yang ditetapkan secara rawak akan mengambil samada alginate anti-asid iaitu [Gaviscon Advance (GA), Reckitt Benckiser, UK] atau anti-asid tanpa alginate iaitu Magnesium Trisilicate [MMT] yang mempunyai kekuatan yang sama selepas makan lewat malam yang telah diselaraskan.

OBJEKTIF

Memantau tahap penurunan "asid pocket", acid refluk dan simptom refluk oleh alginate-anti-asid [Gaviscon Advance (GA), Reckitt Benckiser, UK] formula selepas makan malam berbanding dengan anti-asid bukan alginat dengan menggunakan kapsul tanpa wayar dan pH Impendance dalam peserta gemuk yang tiada simptom GERD setelah mengambil makan lewat malam.

KEPUTUSAN

Perbezaan median pH yang ketara di perut atas dapat dilihat dalam alginate anti-asid kumpulan berbanding dengan anti-asid bukan alginate dengan perbezaan median -2,67 (nilai P 0.008) . Median bilangan dan durasi refluk juga lebih rendah dalam kumpulan alginate anti-asid berbanding alginate anti asid dengan perbezaan median -2.21 dan semua nilai P <0.05. Akan tetapi tiada perubahan dilihat pada pH reflux pada pangkal esophagus iaitu 5 cm di atas spinter esophagus bawah.. Tiada perbezaan dalam parameter refluks (pH , bilangan dan durasi asid refluks) dalam kumpulan anti-asid alginate dengan bukan anti-asid alginate (semua nilai P> 0.05).

KESIMPULAN

Berbanding dengan anti-asid bukan alginat, anti-asid alginate menujukkan penurunan secara ketara “acid poket” di dalam perut atas ,penurunan bilangan dan durasi refluk selepas makan lewat malam .Walaubagaimanapun kajian ini menujukkan tiada perubahan pH yang berlaku di esophagus atas (5 cm diatas spinter esophagus bawah), Ini mungkin disebabkan peranan utama antiasid alginate adalah mengalih “acid pocket” ke tepi dan bukannya menghalang acid refluk dari berlaku seperti yang dilaporkan sebelum ini.

CHAPTER 1

1.0 Introduction

Gastroesophageal reflux disease [GERD] is defined as a chronic state caused by the retrograde flow of gastric contents into the esophagus causing lot of signs and symptoms including abdominal pain,regurgitation and it may cause cardiac like angina pain. Some mechanisms have been postulated to be the related between GERD and obesity, however the data relating the etiologic factors to reflux disease and obesity are conflicting. Changes in diet, prescription medication use, smoking, and alcohol intake and the declining prevalence of *Helicobacter pylori* infection have been suggested [32-33]. Studies have hypothesized that the increasing trend of obesity in western populations has paralleled the increase in esophageal adenocarcinoma, suggested that this trend may be an important factor in this change [34-35]. It is a condition of great medical and social impact due to its increasing number of incidence, causing long-term symptoms and furthermore causing significant impact and affect the patients' quality of life.

The majority of acid reflux episodes occur after meals but paradoxically because this is the period when intragastric contents are at their least acidic owing to the buffering effect of food [13]. The discrepancy between gastric pH and refluxate pH after meals prompted the discovery of the 'acid pocket', an area of unbuffered, highly acidic gastric secretion that accumulates post-prandially in the proximal stomach [13].

Alginate formulations have a "rafting" mode of action that allows them to directly target the acid pocket that demonstrated could eliminate or displace the acid pocket away from the GEJ in GERD patients [81]. However there were no established study assessing the acid pocket suppression by Alginate formulation in association with refluxate and symptoms of GERD. Another study suggested that alginate formulation causes the displacement of acid pocket to a side rather than preventing the reflux per se [82]. The study outcome was conflicting regarding asscociation between acid pocket supression in relation to reflux episodes.

1.1 Definition of obesity

Obesity is defined as a condition of abnormal or excessive fat accumulation in adipose tissue.Obese individuals differ not only according to the degree of excess fat, which they store, but also in the regional distribution of the fat within the body. Indeed, excess abdominal fat is as great a risk factor for disease as it is excess body fat per se [WHO 1998]. One of the most commonly used indices of relative weight is the Body Mass Index [BMI], which is defined as body weight in kilogram divided by height, in meters squared. It was not originally intended as an index of obesity but is now commonly employed as such in epidemiological studies, to predict obesity-related morbidity and mortality in adults.

1.2 Stratification of BMI in Asia Population

The BMI cut-off points for determining overweight and obesity in Asian populations are changing. The population level of BMI cut-off points is to identify risks of adverse health outcomes associated with different levels of body composition, so as to inform and trigger policy action, facilitate prevention programmes and to measure the impact of interventions. For clinical applications, population specific cut-off points will be needed to be determined by countries as the most appropriate and should be used with an individual's clinical history and other clinical measurements (e.g. waist circumference and presence of other related factors). Ethnic-specific cut-off points may not be useful as it is likely to create great confusion in health promotion and disease prevention and management.

A BMI of 30 kg/m^2 is considered the threshold of obesity. For many Asian populations, additional trigger points for public health action were identified as 23 kg/m^2 or higher, representing increased risk, and 27.5 kg/m^2 or higher as high risk. The suggested categories are as follows: less than 18.5 kg/m^2 is underweight, 18.5-23 kg/m^2 is increasing but acceptable risk, 23-27.5 kg/m^2 is increased risk, and 27.5 kg/m^2 or higher is high risk.

It has become increasingly clear that there is an emerging increase in the prevalence of Type 2 Diabetes Mellitus and cardiovascular risk factors in parts of Asia below the cut-off points of less than 25 kg/m^2 for overweight and BMI less than 30.0 kg/m^2 for obesity. (Ko et al. 1999; Deurenberg 2001; China Obesity Task Force 2002; Yajnik 2002; Zhou 2002). Obesity is associated with several chronic diseases and has been implicated as an important risk for the development of GERD and its complications [38].

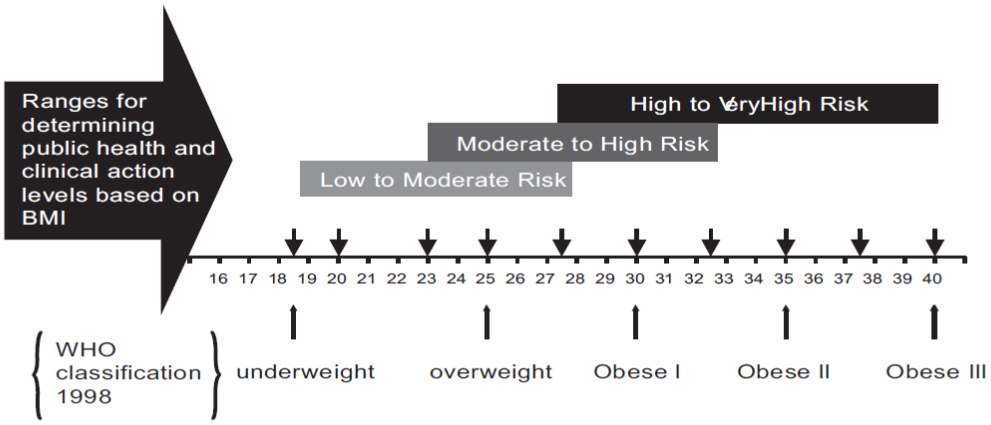

Figure 1: Suggested cut-off points (↓) for reporting population BMI distribution and specific action levels for population and individuals

Source: WHO (2004)

1.3 Prevalence of GERD

The prevalence of GERD and obesity have increased significantly over the past 40 years in Western populations [37]. A study interviewed subjects as part of the German National Health Interview and Examination Survey reported that 18% of the general population suffered from GERD [36]. The prevalence of obesity has been increased from 15% to 33% in adults, and from 6% to 19% in children. Although the diseases are relatively less common among the population in Malaysia previously [2], recent data have suggested an increasing prevalence of reflux disease largely a result of obesity [3,4]**.** Obesity is probably the greatest threat to humankind not just presently but also the coming years. The worldwide prevalence of obesity (BMI $\geq$ 30 kg/m^2) almost doubled with 10% of men and 14% of women in 2008 compared to 5% of men and 8% of women in 1980 [6]. Malaysia did not escape the epidemic, with a national prevalence of 11.7% in those aged 15 years and above in 2004 compared to data from the Second National Health and Morbidity Survey (NHMS) of 4.4% in 1996 [7]. The more recent third NHMS reported a prevalence of 7.4% in men and 13.8% in women [8].

1.4 THE PATHOPHYSIOLOGICAL MECHANISMS OF GERD IN OBESITY

The pathophysiological link between obesity and GERD has not been fully understood. It may be due to general factors such as visceral adiposity, oestrogen levels,or decrease of *Helicobacter pylori* infection with increased gastric acid secretion. Increased abdominal pressure leads to disruption of the GEJ and hiatal hernia, and esophageal motility may be modified by obesity.

The excess in esophageal acid exposure in obesity is because of many factors and mostly due to raised intra-abdominal pressure which in turn increases transient lower esophageal sphincter (LES) relaxations, causes mechanical disruption of the GEJ and leading to early stages partial hiatus hernia and then permanent hiatal hernia in the later stages [1,3]. Esophageal exposure to acid and related gastro-esophageal reflux symptoms are more frequent in the postprandial period. On one side, reflux episodes increase in the postprandial period because of the more frequent occurrence of transient lower esophageal sphincter relaxations.On the other, meals would be expected to reduce the effect of the gastric juice by increasing pH through their buffering effect and thus decrease perception of reflux.

The frequency of transient LES relaxations (TLESR) was increased in obese participants. Obese individuals had a significantly higher rate of TLESRs period after meal ingestion and the proportion of TLESRs accompanied by acid reflux and the total acid exposure times were significantly higher in obese and overweight subjects [40]. A direct correlation between rising BMI increased number of TLESRs and an increased number of TLESRs associated with acid reflux was identified [38-40]. The prevalence of hiatal hernia was increased in obese participants and it is commonly associated with symptomatic GERD, and patients with abnormal esophageal acid exposure have a significantly higher prevalence of hiatal hernia [41]. A study found that the pressure morphology along the EGJ is altered with obesity in a manner supporting the formation of a hiatal hernia [47].

An increase prevalence of esophageal motor disorders in obese participants and the findings were similar and included nonspecific motility disorder and hypotensive LES pressure. The frequency of esophageal motor abnormalities reported is considerably higher than expected relative to nonobese, non-GERD individuals [48-51]. Finally obesity also has shown elevated intragastric pressure in patients which has also been implicated as a contributing factor of GERD [42].

1.5 Nocturnal reflux of GERD and the complication of GERD

The GERD symptoms frequently happen at night and seem to be worse at night compared to daytime symptoms.Out of 1000 adults with heartburn, 79% of respondents experienced symptoms worse at night and 75% of the respondents with night time heart burn said that symptoms affected their sleep and another 40% believed that the symptoms affected their ability to function the following day [20].Almost 11 fold increased of relative risk among persons with nocturnal reflux symptoms, showing a strong association between the two conditions [22].Another survey showed that persons with nocturnal GERD had experienced pain similar to persons with angina and congestive heart failure [21]. Both study showed that nocturnal GERD have a substantial impact on quality of life,this is supported by another study revealed the nocturnal GERD is worse compare to daytime symptom and they appear to be more severe. Nocturnal events are more prolonged and therefore expose the esophagus to acid for a longer period of time [23, 24].

For most individuals, modest size snacks during late evening hours or supper may not be detrimental. However, in Asia, due to long working hours, many individuals tend to eat late with habitual late night supper shortly before bedtime. Such high energy intake at night may increase the risk of obesity and diabetes mellitus [10,11]. Although it is thought that heavy late night supper increases the risk for GERD but no studies have been done. It is also assumed that heavy individuals may have higher risks for GERD if they were to have late meals.Anectodal reports from personal clinical practice suggest that it is a common practice for certain patients to take antacids if they developed symptoms following heavy or late-night meals.

A data described a dose-dependent relationship between increasing BMI and frequent reflux symptoms [52-54]. The GERD symptoms was more frequent and double for obese women compared to normal weight individuals. Another study also showed that an increase in BMI of more than 3.5 in women with normal BMI at baseline increased the risk of GERD symptoms.

The risk for these disorders seems to progressively increase with increasing weight, increasing BMI was positively correlated with increasing esophageal acid exposure, obese patients are more than twice as likely to have a mechanically defective LES[19]. Obese individuals also have more acid reflux episodes, longer reflux time and a greater time pH<4 besides having more reflux symptoms [9].

Obesity is associated with a significant increase 3 times higher in the risk for erosive esophagitis, and esophageal adenocarcinoma[5]. GERD and its complications of Barrett's oesophagus and oesophageal adenocarcinoma have increased markedly in recent decades, not just in the developed countries but also in Asia [1].Studies have also hypothesized that the increasing trend of obesity in western populations has paralleled the increase in esophageal adenocarcinoma and may be an important factor in this change [34-35].

1.6 The concept of acid pocket and pathogenesis of GERD

The acid pocket in the proximal part of stomach after meals has been shown in recent years to be an important mechanism of GERD [6]. The pathogenesis of GERD suggested the escape of normal buffering of a large fatty meal that the region just distal to the esophagogastric junction. [17]. This acid pocket occurred as a result of meal-stimulated acid mixing poorly with the chyme in the proximal stomach.The concept of the "acid pocket" emerged from the observation that postprandial reflux episodes achieved nadir pH values lower than the corresponding values in the gastric body where acidity was buffered by the meal. Another observation study showed that newly secreted acid layered on top of the ingested meal emerged as the explanation for this paradox, based on studies in dyspeptic patients and healthy volunteers [61]. Furthermore, the proximal extent of this acidity extended close to or even proximal to the squamocolumnar junction (SCJ) in the postprandial period. Subsequent observations suggested this effect was more pronounced in patients with GERD and in those with large hiatal hernias [62,63]. The correlation between the pH within the acid pocket and the esophageal nadir pH which is they concluded that the refluxes origins from the the gastric acid pocket [73] and its could have major implications in GERD pathophysiology.

The acid pocket most frequently occur in the first postprandial hour and it also correlates well with the prevalence of postprandial acid reflux events, which are reported to, in both healthy volunteers and GERD patients [74]. Continuous pH monitoring using Bravo capsule found the median time for onset of the acid pocket was 14 min. A number of other studies have demonstrated that the pocket persists for up to 90 min postprandial [73,74]. In one study, real-time recording of fasting and postprandial luminal pH with a 12 electrode assembly allowed close observation of the dynamic changes to esophageal and stomach pH over time .Recordings clearly demonstrated that the gastric cardia paradoxically became more acidic after a meal while the rest of the stomach became less acidic. In this case, the acid pocket was first observed 17 min after the meal, progressively lengthening and becoming more acidic until 44 min . At 48 min, a highly acidic esophageal reflux event was observed at a time when the only region of the stomach with equal acidity was the acid pocket [73-77].

Numerous studies have been conducted to show the existence of acid pocket using different techniques, including pH pull-through catheter.Stepwise pH pull-through from the proximal stomach into the oesophagus revealed that, while intragastric pH increased after a meal (from pH 1.4 to pH 4.4), it remained highly acidic (pH 1.6) in the region adjacent to the GEJ [64]. A lot of image studies had been used to visualise the acid pocket eg multiple stationary pH electrodes single-photon emission computed tomography following injection of [^{99M}Tc] pertechnetate and, magnetic resonance imaging(MRI) [64,65,66,67].

1.7 Acid Pocket and Hiatus Hernia

Hiatus hernia causes LES function become impaired, thereby its increasing esophageal acid exposure is involved in the pathogenesis of GERD [67,68]. Studies suggested that the presence of hiatus hernia may influence reflux disease through effects on the size and position of the acid pocket. Compared between healthy volunteers and obesity,it demonstrated that reflux patients had longer acid pockets, attributable to the proximal migration of the GEJ owing to hiatus hernia formation. The existence of the acid pocket mainly located above the diaphragm or extended into the hiatal opening. It is confirmed that both the presence of a hiatus hernia and positioning of the acid pocket above the diaphragm were major independent risk factors for acidic reflux to occur during a TLESR. Assuming that the acid pocket migrates upwards with the LES, a situation comparable to a hernia would result promoting acid reflux. In fact, continuous postprandial monitoring of the location of the GEJ in healthy volunteers confirmed that during TLESRs, there was marked proximal movement of the GEJ, representing significant herniation [69]. In line with this, MRI reveals subtle anatomical differences in GERD patients vs. healthy volunteers and they found these changes create structural disruption of the GEJ, albeit in a less severe manner than hiatus hernia.

1.8 TREATMENT of GERD

1.8.1 Proton pump inhibitor (PPI)

Proton-pump inhibitors (PPI) and Histamine 2 antagonist (H2RA) were widely used for the treatment of GERD. Both drugs were potent acid-suppressor agents and they have different pharmacology and pharmokinetic effects[55,56]. H2RA eg ranitidine have a rapid onset of acid-suppressing effects and are effective for acid control but it has been reported that the long-term administration of the drugs causes tolerance of its acid-suppressing effect. Another study found that it causes rebound phenomenon that causes reflux symptom and ulcer recurrence after the stopping of medication [57,58],

PPIs were a group of drugs whose main action is a pronounced and long-lasting reduction of gastric acid production. PPI have more potent and more stable acid-suppressing effects than those of H2RA, but the onset of the effects of PPI occurs much later than that of H2RA [58].Within the class of medications, there was no clear evidence that one agent works better than another .

1.8.2 Antacids

The stomach normally produces acid to help with the digestion of food and to bacteria. This acid is corrosive so your body produces a natural mucous barrier which protects the lining of the stomach from being eroded. In some people this barrier may have broken down allowing the acid to damage the stomach, causing an ulcer. In others there may be a problem with the muscular band at the top of the stomach that keeps the stomach tightly closed. This may allow the acid to escape and irritate the oesophagus and may cause heartburn and/or oesophagitis.

Antacids are preparations that are primarily designed to neutralize gastric acid. The proliferation of antacid formulations includes combinations and varying proportions of a number of basic materials, in an attempt to produce improved neutralization characteristics with lowered untoward effects.

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1.8.2.1 Alginate formulation antacid

Alginate antacid is a alginates based antacid which are natural polysaccharide polymers isolated from brown seaweed (*Phacophycae*). On contact with gastric acid, alginate precipitates into a low density viscous gel of near neutral pH in a matter of seconds in vitro or a few minutesin vivo[59]. Once the pH change, the sodium bicarbonate contained in the alginate-antacid formulation releases carbon dioxide, which is then trapped in the alginate gel causing it to float to the top of the gastric contents like a "raft" [60]. Hence, alginate-based formulations with sodium bicarbonate may effect direct and immediate neutralization of the acid pocket film. Alginates are added to help protect and prevent from stomach acid and they are present in antacid medications with various brand names. Alginate-antacid based on the concept of forming a raft on top of gastric content.

The combination antacid-alginate preparation is recently shown to be more effective in relieving postprandial acid pocket and reflux events [12,13]. Gaviscon Advance (GA; Reckitt Benckiser) is a Alginate–antacid formulations which contains three active ingredients: sodium alginate, sodium bicarbonate and calcium carbonate. Gaviscon® is probably good for symptom relief after a heavy late supper especially in obesity. The Gaviscon have a number of advantage that make them candidates for protection from acid reflux. They form a highly viscous 'raft' that floats at near the GEJ junction and ideally to counteract the 'acid pocket'that formed on the top of the meals, it is also known to be effective by forming a physical barrier to reflux for up to 4 h and hence able to neutralise gastric acid [25-28]. Alginate preparations have also been shown to be more effective than placebo and as effective as acid suppressant medication for short-term symptomatic control of GERD [29,30]. Another study demonstrated that an alginate/antacid combination neutralized the acid layer on top of a meal and profoundly shifted the pH transition point away from the GEJ in the majority of GERD patients studied[83].

1.8.2.2 Non alginate antacid

Non alginate antacid is another type of antacid that had been used for GERD for long period of time before existence of Alginate antacid and PPI. It is commonly available over the counter as a form of medicine for quick relief of GERD symptoms for most people. Antacids are a group of medicines which help to neutralise the acid content of your stomach. Antacids include aluminium hydroxide, magnesium carbonate and magnesium trisilicate. These come in various brand names and are available as tablets and liquids.Some antacids are combined with another medicine called simeticone which helps to reduce flatulence.

1.9 pH Acid Monitoring and Evaluation

The best objective methods to demonstrate the presence of acid reflux are conventional ambulatory catheter pH monitoring and the Bravo capsule catheter-free pH test [6-8]. Both methods are valid and reliable for the measurement of esophageal acid exposure Ambulatory 24-h esophageal pH monitoring is considered to be the gold standard to diagnose GERD but catheter-based pH testing has limitations including issues of sensitivity, specificity, tolerability and the inability to record non-acid reflux events not until the recent addition of impedance [14].

On the other hand, the Bravo® wireless technology has been validated in several studies, with improvements over the catheter-based pH monitoring in terms of better tolerability with probable equal accuracy as well as the ability to record periods both off and on PPIs therapy over a prolonged period of time [15,16]. There were no differences between the pH data obtained with the pH probe catheter and the Bravo capsule where the pH probe and Bravo™ capsule were placed simultaneously.[17.18]

The method of placement Bravo capsule at gastric cardia is shown to be feasible for pH monitoring and showed successful placement and interpretable recording for >42 h [18].This is a novel placement method in asesssing the acidity distal to GEJ which is found as an “unbuffered area” or acid pocket that is speculated as an important pathogenesis of non-erosive reflux disease.

CHAPTER 2

2.0 Hypothesis

Alginate-antacid preparation suppresses post-supper acid pocket, night-time acid-reflux and symptoms more effectively than antacid in obese participants.

2.1 Null hypothesis

There is no difference in acid pocket suppression post meals between groups alginate-antacid and non alginate antacid in obese participants.

Conceptual Framework is as attached (Appendix A)

2.2 Specific objectives

1. To compare the acid-pocket patterns, night-time pH patterns and **symptoms between alginate-antacid preparations vs antacid** in obese participants after taking late-night supper.

2. To compare the acid pocket patterns, night time pH patterns and symptoms **with vs. without alginate-antacid preparation** in obese participants after taking late night supper.

3. To compare the acid pocket patterns, night time pH patterns and symptoms **with vs. without antacid alone** in obese participants after taking late night supper.