Received: 27 February 2020 | First decision: 10 March 2020 | Accepted: 2 April 2020

DOI: 10.1111/apt.15746

AP&T Alimentary Pharmacology & Therapeutics WILEY

Randomised clinical trial: the effectiveness of Gaviscon Advance vs non-alginate antacid in suppression of acid pocket and post-prandial reflux in obese individuals after late-night supper

Mohd Adli Deraman[1] | Muhammad Ilham Abdul Hafidz[2] | Rona Marie Lawenko[3] | Zheng Feei Ma[1,4] | Mung Seong Wong[1] | Cathal Coyle[5] | Yeong Yeh Lee[1,6,7]

[1]School of Medical Sciences, Universiti Sains Malaysia, Kota Bahru, Malaysia

[2]Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Malaysia

[3]De La Salle Health Sciences Institute, Dasmarinas, Philippines

[4]Department of Health and Environmental Sciences, Xi'an Jiaotong-Liverpool University, Suzhou, China

[5]Reckitt Benckiser, Slough, UK

[6]Gut Research Group, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

[7]St George and Sutherland Clinical School, University of New South Wales, Sydney, NSW, Australia

Correspondence
Yeong Yeh Lee, School of Medical Sciences, Universiti Sains Malaysia, Kota Bahru, Malaysia.
Email: justnleeyy@gmail.com

Funding information
The study was funded by Reckitt Benckiser (M) Sdn. Bhd. The funder had no role in study design, data collection and analysis and decision to publish.

Summary

Background: Late-night supper increases the risk of postprandial reflux from the acid pocket especially in obesity. An alginate-based, raft-forming medication may be useful for obese patients with GERD.

Aims: To compare the efficacy of Gaviscon Advance (Reckitt Benckiser, UK) and a non-alginate antacid in post-supper suppression of the acid pocket and post-prandial reflux among obese participants.

Methods: Participants underwent 48 h wireless and probe-based pH-metry recording of the acid pocket and lower oesophagus, respectively, and were randomised to single post-supper (10 PM) dose of either Gaviscon Advance or a non-alginate antacid on the second night. Primary outcomes were suppression of median pH of acid pocket and lower oesophagus, measured every 10-minutes post-supper for 1 h. Secondary outcomes were suppression of % time pH < 4 at lower oesophagus and improvement in frequency and visual analogue score (VAS) of regurgitation.

Results: Of the 81 screened participants, 55 were excluded and 26 (mean age 33.5 years, males 77.8% and BMI 32.8 kg/m^2) were randomised to Gaviscon Advance (n = 13) or antacid (n = 13). Median pH of the acid pocket but not the lower oesophagus was suppressed with Gaviscon Advance vs antacid (all $P < 0.04$) Gaviscon Advance but not antacid significantly reduced in % time pH < 4, symptom frequency and VAS on day 2 vs day 1 (all $P < 0.05$).

Conclusions: Among obese individuals, Gaviscon Advance was superior to a non-alginate antacid in post-supper suppression of the acid pocket. (Clinical trial registration unique identifier: NCT03516188).

The Handling Editor for this article was Dr Colin Howden, and it was accepted for publication after full peer-review.

1 | INTRODUCTION

In the last decade, gastro-oesophageal reflux disease (GORD) and its complications of Barrett's oesophagus and oesophageal adenocarcinoma are increasingly prevalent, especially in Asia.[1,2] The rise in GORD among Asians is largely attributed to a recent increase in the prevalence of obesity.[3,4] Based on nationally representative data from countries in the Asia Pacific, the combined crude obesity rate ranged from 5% in India to 60% in Australia.[5] Malaysia is the most obese country in South East Asia, and according to its Third National Health and Morbidity Survey (NHMS) report in 2010, the prevalence of obesity was 7.4% in men and 13.8% in women.[6]

We have previously shown that physiological dysfunction of the gastro-oesophageal junction (GOJ) in the form of partial hiatus hernia may explain the excess distal oesophageal acid exposure in obesity.[1,3] Acid pocket, an area distal to GOJ that escape normal buffering of a meal, is a reservoir of acid that readily refluxes[7] but it also expands in the presence of a hernia. Unlike the usual antacid or proton-pump inhibitor (PPI), alginate-based reflux suppressants, including Gaviscon Advance, have the capability to displace the acid pocket but also form a physical barrier against reflux through formation of alginate raft at the GOJ.

GORD symptoms frequently happen at night but may also have a higher impact at night compared to daytime[8] due to loss of usual physiological function associated with sleep and the supine position.[9] In many Asian countries including Malaysia, because of long working hours, many individuals tend to eat late or with habitual late-night supper shortly before bedtime. It is possible that the acid pocket formed after supper may persist or even expand due to sleeping position causing more night-time reflux, and when coupled with loss of physiological protection during sleep would therefore lead to worse GORD over time.[10,11] Antacids eg, Eno, easily available over-the-counter in Asia, are often taken by individuals following heavy or late-night meals. However, these typical antacids may not be effective or durable for night-time reflux in the presence of expanded acid pocket or in obesity where there is already a dysfunction of the GOJ.

Therefore, the aim of this study was to investigate the effectiveness and mechanistic advantages of Gaviscon Advance over non-alginate antacids in suppressing acid pocket and post-prandial reflux in obese participants following a heavy late-night supper.

2 | MATERIALS AND METHODS

2.1 | Study eligibility and design

This was a randomised controlled trial conducted between June 2016 and July 2017 at Hospital Universiti Sains Malaysia (USM), a tertiary academic centre at the northeastern Peninsular Malaysia. Inclusion criteria were healthy but obese participants (BMI ≥ 27.5 kg/m^2) without clinically significant medical conditions involving the cardiovascular, neurological, pulmonary, renal, gastrointestinal, hepatic, metabolic, endocrine or haematological system. Exclusion were those with prior gastrointestinal (GI) conditions that required ongoing treatment, GORD Questionnaire (GORDQ) score < 8 (low probability),[12] recent (past 2 months) use of proton-pump inhibitor or other antacids, previous history of abdominal surgeries, upper GI disorders found during endoscopy and manometry and failure to place Bravo capsule and/or to insert the pH-impedance catheter. All participants were recruited by one of the researchers (MAD).

This randomised controlled trial was approved by the USM Human Research Ethics Committee (JEPEM code approval: USM/JEPEM/15020071) and signed informed consent was obtained from all participants. This study was registered with ClinicalTrials.gov (unique identifier NCT03516188). In addition, this study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement and Declaration of Helsinki.

2.2 | Study protocol and intervention

At baseline, information on age, sex, weight, height, waist circumference (WC) and GORDQ were obtained. Eligible obese participants were then randomised to receive either the Gaviscon Advance (Reckitt Benckiser, UK) or non-alginate antacid (ie control group) (Figure 1) using a random number table generated from the SPSS version 25 software (SPSS Inc) based on block size of 24 and stratified by treatment. From the random number table generated, if the first entry was "1", then the first participant would be assigned to treatment 1 (Gaviscon Advance). If the next entry was "2", the second participant would be assigned to treatment 2 (non-alginate antacid) so on and so forth.

Each participant would undergo high-resolution oesophageal manometry, followed by upper endoscopy during which the Bravo capsule (Medtronic) would be placed and then the pH-impedance probe inserted. Recordings of both Bravo and pH-impedance were started simultaneously. All participants would then be hospitalised for the next 2 days (Table 1).

During both days of pH recordings, participants were encouraged to engage their usual daily activities and diets. Also, participants were asked to record their food intake, sleep period and occurrence of any symptoms or adverse events in their diaries. Symptom severity was evaluated based on VAS (0 to 10) and frequency of symptom occurrence following night supper.

On day 1, there was no active intervention other than the late-night supper given at 10:00 PM. The meal consisted of two chicken burgers and a cup of 250 mL milk tea. On day 2, after the same late-night meal, again at 10:00 PM, the alginate group was given 10 mL of Gaviscon Advance and the non-alginate antacid group, 4 mL of 200 mg magnesium trisilicate preparation. Participants were instructed eat the late-night supper at the same pace on both days.

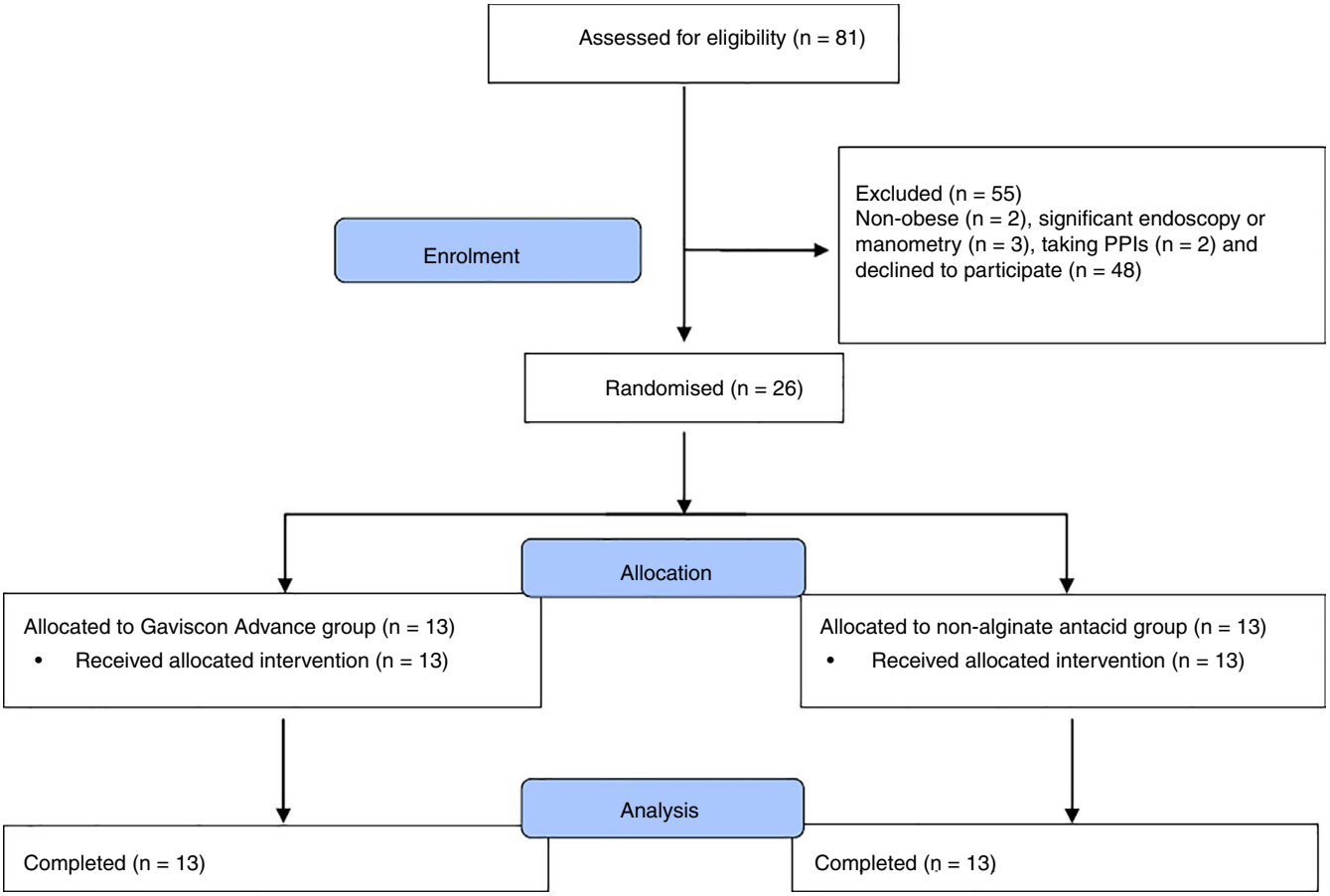

FIGURE 1 Study flow chart

TABLE 1 Demographic and baseline characteristics

Variables	Gaviscon Advance group (n = 13)	Non-alginate antacid group (n = 13)	*P*
Age (years)[a]	34.9 ± 12.2	37.0 ± 13.6	0.7
Weight (kg)[a]	88.8 ± 15.5	87.8 ± 15.6	0.7
Height (m)[a]	1.63 ± 11.3	1.63 ± 8.1	0.9
Waist circumference (cm)[a]	101.9 ± 16.8	102.7 ± 12.4	0.8
BMI (kg/m^2)[a]	33.2 ± 4.8	33.2 ± 6.8	0.7
GORDQ score[b]	7.0 (6.5, 8.5)	7.0 (6.0, 10.0)	0.8
Symptom frequency[b]	1.8 (0.0, 5.6)	0.0 (0.0, 1.0)	0.02
VAS score[b]	2.5 (0.0, 12.5)	0.0 (0.0, 2,5)	0.04
pH values at acid pocket[b]	4.6 (3.9, 5.9)	5.0 (4.7, 5.9)	0.3
pH values at lower oesophagus[b]	6.3 (5.1, 6.8)	6.2 (5.9, 6.4)	0.9
% time pH < 4 at lower oesophagus[b]	2.5 (0.0, 5.8)	0.0 (0.0, 5.4)	0.04

Abbreviation: VAS, visual analogue scale.

[a]Mean ± SD

[b]Median pH (25th and 75th percentiles)

2.3 | Study procedures

2.3.1 | High-resolution esophageal manometry

A solid-state probe (Laborie Medical Technologies) that consists of 36 pressure channels and 8 impedance sensors was placed across the oesophagus and upper stomach of participants. The catheter was inserted nasally after lignocaine spray in the sitting position. After rest, participants were given 10 5-mL water swallows. Upon completion of all water swallows, the probe was removed. The upper border of lower oesophageal sphincter (LOS) was measured during rest period, and participants with major motility disorders especially achalasia were excluded from study.

2.3.2 | Upper endoscopy and Bravo capsule insertion

After an overnight fast, participants underwent an upper endoscopy (Model GIF-140 and GIF-160; Olympus Medical Systems) performed by a single endoscopist (YYL) with either local lignocaine spray or low dose sedation (midazolam or fentanyl). Participants with erosive oesophagitis, peptic ulcer disease and malignancies found during endoscopy would be excluded from the study and managed accordingly.

The Bravo capsule was inserted orally using a delivery device under endoscopy guidance as previously described.[13] Usually, the Bravo capsule is placed 6 cm above the squamous-columnar junction (SCJ) but in our study, we placed the capsule at the cardia where the acid-pocket is situated, based on the technique previously published.[14] The attachment well of the Bravo capsule was positioned immediately proximal to the SCJ. In this position, the pH sensor of capsule would be positioned 1.5-2 cm distal to the SCJ.[14] Once capsule was locked in place typically there was little (chest discomfort) or no discomfort. Participants were asked to carry a recording device around their waist for the next 48 hours.

2.3.3 | Ambulatory pH-impedance monitoring

The ComforTEC pH-impedance probe (Diversatek Healthcare) consists of one pH sensor located 5 cm from the tip of catheter, and 6 regularly spaced impedance sensors. After endoscopy, the probe was inserted nasally in the sitting position and the pH sensor was placed 5 cm above the upper border of LES determined from manometry. Once the pH sensor was in its correct location, recording with the ZepHr system (Diversatek Healthcare) would start simultaneously with the Bravo capsule. Participants were asked to carry a recording device around their waist for the next 48 hours and were given additional batteries to allow extended recording.

2.4 | Data and statistical analysis

Due to the exploratory nature of study and lack of previous data, sample size was not calculated. Recorded data in the text format from both Bravo and the ZepHr system were exported to Microsoft Excel (Microsoft Corp.) and SPSS software for further analysis. All pH data analysis was performed blinded to therapeutic groups by two investigators independently (MAD and ZFM). Unless indicated otherwise, all continuous data were reported as median (interquartile range). From the Bravo capsule data of the cardia, median pH values were derived at every 10 minutes interval for an hour following supper. From pH data of the lower oesophagus, median pH values and % time pH < 4 were obtained every 10 minutes for an hour following supper. Primary outcomes were suppression of median pH values of acid pocket and lower oesophagus. Secondary outcomes were improvement in % time pH < 4, reduction in frequency and VAS of post-supper regurgitation.

SPSS 24.0 software (SPSS) was used for statistical analysis. Only per-protocol analysis was performed. Differences in pH and reflux variables were determined between- and within-intervention groups using the Wilcoxon signed-rank test and Mann–Whitney test. For between-group analysis, pH and reflux variables were compared between Gaviscon Advance and non-alginate antacid at 10-min interval following night-supper at day 2. For within-group analysis, pH and reflux variables at 10-min interval following night-supper were compared between day 1 and day 2 in each intervention group.

3 | RESULTS

3.1 | Baseline characteristics

Of the 81 screened adults, 55 failed eligibility criteria including BMI <27.5 kg/m^2 (n = 2), significant endoscopy or manometry findings (n = 3) or were taking PPIs within the last 2 months (n = 2) (Figure 1). There were four (4) participants who initially failed to deploy the Bravo capsule but all eventually succeeded on the second attempt, therefore no patients were excluded due to failure to place capsule or the pH probe. The remaining 26 participants (mean age 33.5 ± 10.6 years, males 77.8%, BMI 32.8 ± 5.7 kg/m^2, WC 102.1 ± 15.9 cm, and median GORDQ 7.0) were randomised either into the Gaviscon Advance group (n = 13) or the non-alginate antacid group (n = 13). Baseline characteristics including median pH values at acid pocket and lower oesophagus were similar between the two groups except for greater symptom frequency, VAS and % time pH < 4 in the Gaviscon Advance group (Table 2).

3.2 | Attachment and tolerability of procedures

Placed capsule were located at the intended position in all participants when observed with upper endoscopy performed after placement. Chest x-ray performed 24-hour after endoscopy also confirmed the location and that the Bravo capsule was in situ. All participants

TABLE 2 Results of between-group differences for other parameters of GERD

Variables	Day 1			Day 2		
	Gaviscon Advance (n = 13)	Non-alginate antacid (n = 13)	*P*-value	Gaviscon Advance (n = 13)	Non-alginate antacid (n = 13)	*P*
% time pH < 4[a]	2.5 (0.0, 5.8)	0.0 (0.0, 5.4)	0.04	0.0 (0.0, 0.8)	0.0 (0.0, 0.0)	0.9
Symptom frequency[a]	1.8 (0.0, 5.6)	0.0 (0.0, 1.0)	0.02	1.0 (0.0, 1.0)	0.0 (0.0, 0.5)	0.1
VAS score[a]	2.5 (0.0, 12.5)	0.0 (0.0, 2,5)	0.04	0.0 (0.0, 2.5)	0.0 (0.0, 1.1)	0.3

[a]Median pH (25th and 75th percentiles)

tolerated both capsules and pH-impedance catheter for 48-hour monitoring without serious adverse effects or any need to remove.

3.3 | Post-supper median pH at the acid pocket

At 10 minutes post-supper day 1, the median pH value was increased but started to decrease at 20 minutes because of acid pocket formation. At day 2, the effect of Gaviscon Advance was observed at 10 minutes after administration. On day 1, no between-group differences in the median pH values were observed at the acid pocket at 10, 20, 30, 40, 50 and 60 minutes following night supper (all $P > 0.05$). However, at day 2, Gaviscon Advance reported higher median pH values than the non-alginate antacid at 20, 30, 40, 50 and 60 minutes post-supper (all $P < 0.04$). For within-group differences (ie day 2 vs day 1), a higher median pH at 10, 20, 30, 40, 50 and 60 minutes post-supper was observed with Gaviscon Advance but not with non-alginate antacid (all $P < 0.003$) (Figure 2A) except at 40 minutes ($P = 0.023$) (Figure 2B).

3.4 | Post-supper median pH at the lower oesophagus

Unlike the acid pocket, no between-group differences (ie Gaviscon Advance vs antacid group) in the median pH values were observed at 10, 20, 30, 40, 50 and 60 minutes following night supper (all $P > 0.05$). Similarly, neither were within-group differences (ie day 2 vs day 1) observed in the median pH values with Gaviscon Advance (Figure 2C) nor the non-alginate antacid (Figure 2D) (all $P > 0.05$).

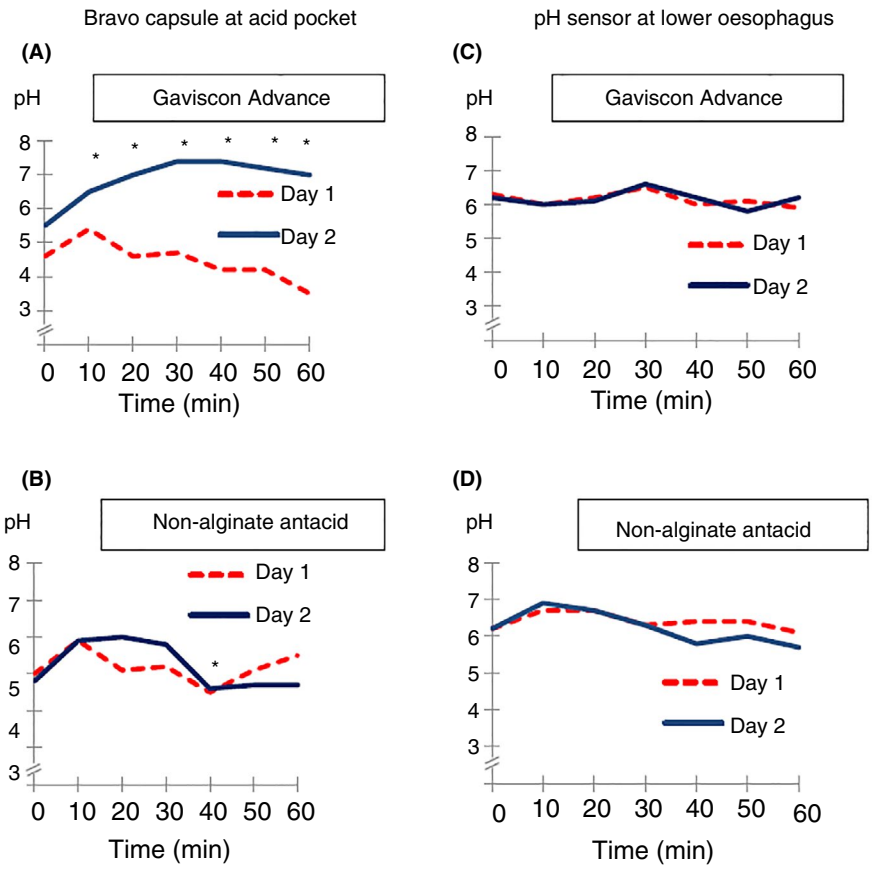

FIGURE 2 Post-supper median pH values of the acid pocket on day 1 and day 2 were illustrated for (A) Gaviscon Advance group and (B) non-alginate antacid group. For median pH values of the lower oesophagus, these were illustrated as (C) for the Gaviscon Advance group and (D) for the non-alginate antacid group. Asterisks above data points indicate significant differences in median pH between day 1 and day 2 for each group ($P < 0.05$)

3.5 | Post-supper % time pH < 4 at the lower oesophagus

Only obese participants in the Gaviscon Advance but not the non-alginate group reported higher % time pH < 4 at day 1 (2.5 vs 0, P = 0.04) (Table 2). On day 2, after administration of Gaviscon Advance, participants reported lower % time pH < 4 (P = 0.04).

3.6 | Symptom responses

Even though at baseline the GORD risk and median pH were similar between intervention groups, the post-meal symptoms were not. At baseline or day 1, obese participants randomised into the Gaviscon Advance group had more regurgitation including higher frequency (1.8 vs 0, P = 0.02) and greater VAS scores (2.5 vs 0, P = 0.04) (Table 2). A greater symptom improvement was observed at day 2 vs day 1 after administration of Gaviscon Advance (ie P = 0.02 and 0.01 for frequency and VAS score respectively).

4 | DISCUSSION

We demonstrated that it was feasible to have the Bravo capsule placed at the cardia (or acid pocket) alongside pH-impedance catheter with a continuous recording over 48 hours. There were no reported adverse events from participants and no early capsule dislodgment, or its removal needed during the period of recording. A previous study has reported placement of two Bravo capsules, one at the gastric cardia and another at distal oesophagus but such a methodology was too expensive in our setting.[14]

At 10 minutes post-supper, the pH values of the gastric cardia were found increased because of buffering effect of the meal. However, pH values started to decrease at 20 minutes post-meal because of the acid pocket.[15] The above observation confirmed that our placed Bravo capsule in gastric cardia was indeed recording the acid pocket. In addition, our study observed that the effect of Gaviscon Advance on the acid pocket begun as early as 10 minutes after meal. Bravo capsule may be a more precise technique than MRI in determining the onset of acid pocket formation (approximately 14 minutes post-meal with MRI)[16] but also the onset of treatment effect from alginate. Furthermore, in our study, Gaviscon Advance was able to sustain its action without any loss of effects throughout the entire hour of recording after supper (Figure 2). Several studies have demonstrated that the acid pocket persists for up to 90 minutes post-meal and the drug effect of alginate may last for approximately 4 hours.[17]

Among the current therapies for GORD, Gaviscon Advance has been shown to reduce symptoms effectively, both as monotherapy and as add-on therapy with PPIs for breakthrough symptoms.[18,19] However, the exact mechanisms how this compound work are not entirely clear. From imaging studies, the alginate in formulation is found to form a physical barrier at the GOJ and that it also displaces the acid pocket away from the GOJ.[20,21] However, despite the alginate action on acid pocket, studies by Sweis et al,[21] Kwiatek et al[22] and De Ruigh et al[23] did not demonstrate an effect on pH at the lower oesophagus and also the number of proximal refluxates.

Overall, our study supported the findings of Kwiatek, Sweis and De Ruigh et al with some differences.[21-23] Following supper, with Gaviscon Advance, we have described that the acid pocket was suppressed earlier and more effectively (pH > 7) unlike the non-alginate antacid (Figure 2). However, we did observe a partial pH suppression effect of non-alginate antacid on the acid pocket albeit not effectively above pH 7. We postulate that both Gaviscon Advance and non-alginate antacid were pushed more proximally into the acid pocket area due to the increase in intra-abdominal pressure from obesity (Figure 3). While both agents were closer to acid pocket, Gaviscon Advance was more effective than antacid in suppressing the acid pocket.

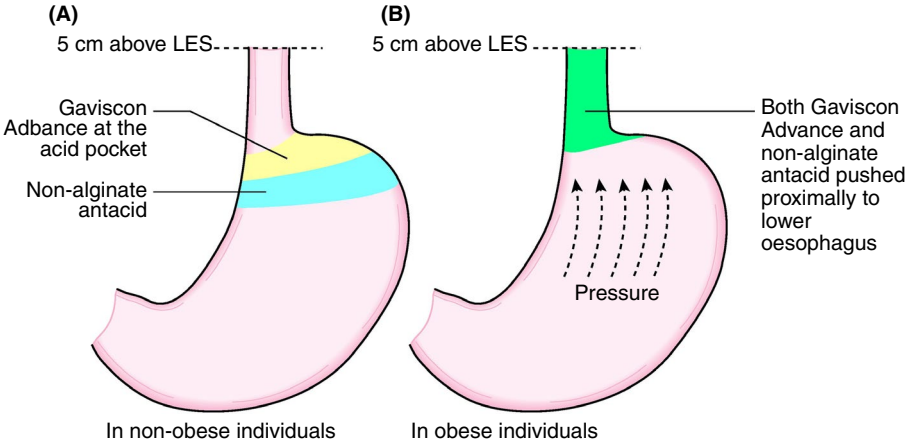

FIGURE 3 Illustration to explain the observed effects in the post-supper median pH of acid pocket and lower oesophagus for Gaviscon Advance and non-alginate antacid. In non-obese individuals, Gaviscon Advance lies at the area of acid pocket but antacid below the acid pocket (A), however, in obese individuals, due to increased intra-abdominal pressure after meal, both Gaviscon Advance and non-alginate antacid would be pushed up to neutralise acid reflux at lower oesophagus (B)

Similarly with Kwiatek, Sweis and De Ruigh et al's papers,[21-23] we did not report a significant difference between Gaviscon Advance and non-alginate antacid on the suppression of pH values at the lower oesophagus. It is not understood why this was so but several postulations are possible. First, we postulated that due to obesity, both agents are displaced more proximally into the cardia but also the lower oesophagus (Figure 3). Second, because of the proximal displacement also, refluxes of both compounds into the distal oesophagus are thus more likely. Third, because of obesity is associated with partial hiatus hernia, a phenomenon we have previously reported,[3] both the proximally displaced compounds are more likely trapped and therefore exert greater clinical effects. Further studies are needed to confirm our postulations but a recent study in pregnant women which reported similar symptomatic benefits between alginate vs non-alginate antacids may have supported our hypothesis.[24]

We noted there were more obese participants with post-meal regurgitation in the Gaviscon Advance group but not in the non-alginate group. This is likely incidental since at baseline, all participants were low probable for GORD however low probable risk does not mean absence of post-meal reflux symptoms. Since Gaviscon Advance was given only in day 2, the observed improvement in symptom in addition to reduction in % time pH < 4 indicated that in symptomatic obese individuals, Gaviscon Advance is effective. Additionally, given the complications of GORD in obesity including Barrett's oesophagus and adenocarcinoma, Gaviscon Advance is likely more attractive than antacids because of its mucosal protection effects. Recent in vitro studies have shown that alginate helps to preserve the oesophageal mucosa integrity and prevents the superficially located mucosal afferent from exposure to acid solutions.[25,26] If proven in human studies, the protective effects of alginate would have better and more durable clinical benefits.

Our study has several unique strengths but also limitations. (a) Our population consisted of obese participants with a relatively large BMI (mean 33 kg/m^2) and WC (mean 102 cm) for Asians. While inclusion of obese population provided us a unique opportunity to study this high-risk group, but it also constituted a limitation to our sample size. In addition, the inclusion of participants with greater symptom frequency, VAS and % time pH < 4 in the Gaviscon Advance group might have more refluxes and would therefore be less likely to respond to treatment. (b) We had utilised Bravo capsule to record the acid pocket and a stationary pH-impedance probe to record the lower oesophagus, a first in the literature, but our study eligibility was affected by high costs, technical challenges and adverse events associated with these procedures. (c) Late-night supper, a unique food habit among many late-working Asians, was provided as the meal challenge. Again, this allowed us to study the potential adverse effects associated with what we assumed as an "unhealthy" food practice, but participants needed an overnight admission at the hospital in order to administer the meal. (d) Gaviscon Advance was compared to non-alginate antacid in a randomised design. However, two-thirds of potentially eligible participants were not randomised, obviously due to our challenging methodology, and thus limit the generalisability of our study. In addition, on retrospect, participants should have been randomised based on evaluation of day 1 post-meal symptoms rather than solely on the risk probability of GORD at baseline. (e) Both compounds were administered only once ie only on day 2 and did not have the same compounds and volume albeit similarity in flavour and strength. (f) Due to our study objectives, the assessment of acid exposure was limited to the first 60 minutes post-meal but we acknowledge a longer lasting acid exposure would be expected after a late-night supper.

In conclusion, among obese subjects after a late-night supper, Gaviscon Advance is more effective than non-alginate antacid in the suppression of acid pocket but both are effective for postprandial acid reflux probably because of obesity pushing both compounds proximally.

ACKNOWLEDGEMENT

Declaration of personal interests: Yeong Yeh Lee has received research funding from Reckitt Benckiser and Morinaga Milk Industry, and has served as speaker or consultant or advisory board member for Reckitt Benckiser, Takeda, Servier and Danone-Dumex. Other authors did not have personal interests.

Declaration of funding interests: This study was funded in full by Reckitt Benckiser (M) Sdn Bhd.

AUTHORSHIP

Guarantor of the article: Yeong Yeh Lee.

Author contributions: MAD, MIAH, RML, MSW and YYL participated in study design. MAD, MIAH, RML, MSW and YYL were responsible for study recruitment and data acquisition. MAD, MIAH, RML, ZFM, MSW and YYL conducted statistical analysis and interpreted the data. MAD, ZFM, CC and YYL revised the manuscript.

All authors approved the final version of the article, including the authorship list.

ORCID

Zheng Feei Ma https://orcid.org/0000-0002-7276-2229
Cathal Coyle https://orcid.org/0000-0003-3190-8460
Yeong Yeh Lee https://orcid.org/0000-0002-6486-7717

REFERENCES

1. Lee YY, McColl KE. Disruption of the gastroesophageal junction by central obesity and waist belt: role of raised intra-abdominal pressure. *Dis Esophagus*. 2015;28:318-325.
2. Wang Y-K, Hsu W-H, Wang SSW, et al. Current pharmacological management of gastroesophageal reflux disease. *Gastroent Res Pract*. 2013;2013:983653.
3. Lee YY, Wirz AA, Whiting JGH, et al. Waist belt and central obesity cause partial hiatus hernia and short-segment acid reflux in asymptomatic volunteers. *Gut*. 2014;63:1053-1060.
4. Robertson EV, Derakhshan MH, Wirz AA, et al. Central obesity in asymptomatic volunteers is associated with increased intrasphincteric acid reflux and lengthening of the cardiac mucosa. *Gastroenterology*. 2013;145:730-739.
5. Asia Pacific Cohort Studies Collaboration. The burden of overweight and obesity in the Asia-Pacific region. *Obes Rev*. 2007;8:191-196.

6. Khambalia AZ, Seen LS. Trends in overweight and obese adults in Malaysia (1996–2009): a systematic review. *Obes Rev*. 2010;11:403-412.
7. Fletcher J, Wirz A, Young J, Vallance R, McColl KE. Unbuffered highly acidic gastric juice exists at the gastroesophageal junction after a meal. *Gastroenterology*. 2001;121:775-783.
8. Shaker R, Castell DO, Schoenfeld PS, Spechler SJ. Nighttime heartburn is an under-appreciated clinical problem that impacts sleep and daytime function: the results of a Gallup survey conducted on behalf of the American Gastroenterological Association. *Am J Gastroenterol*. 2003;98:1487-1493.
9. Jung H-K, Choung RS, Talley NJ. Gastroesophageal reflux disease and sleep disorders: evidence for a causal link and therapeutic implications. *J Neurogastroenterol Motil*. 2010;16:22-29.
10. Morgan LM, Shi JW, Hampton SM, Frost G. Effect of meal timing and glycaemic index on glucose control and insulin secretion in healthy volunteers. *Br J Nutr*. 2012;108:1286-1291.
11. de Castro JM. When, how much and what foods are eaten are related to total daily food intake. *Br J Nutr*. 2009;102:1228-1237.
12. Vadivelu S, Ma Z, Ong E, et al. Clinical validity and reliability of the Malay language translations of gastroesophageal reflux disease questionnaire and quality of life in reflux and dyspepsia questionnaire in a primary care setting. *Dig Dis*. 2019;37:100-107.
13. Lawenko RMA, Lee YY. Evaluation of gastroesophageal reflux disease using the Bravo capsule pH system. *J Neurogastroenterol Motil*. 2016;22:25-30.
14. Pandolfino JE, Schreiner MA, Lee TJ, Zhang Q, Kahrilas PJ. Bravo capsule placement in the gastric cardia: a novel method for analysis of proximal stomach acid environment. *Am J Gastroenterol*. 2005;100:1721-1727.
15. Clarke AT, Wirz AA, Seenan JP, Manning JJ, Gillen D, McColl KE. Paradox of gastric cardia–it becomes more acidic following meals while the rest of stomach becomes less acidic. *Gut*. 2008;58:904-909.
16. Hampson FC, Jolliffe IG, Bakhtyari A, et al. Alginate–antacid combinations: raft formation and gastric retention studies. *Drug Dev Ind Pharm*. 2010;36:614-623.
17. Marciani L, Little SL, Snee J, et al. Echo-planar magnetic resonance imaging of Gaviscon alginate rafts in-vivo. *J Pharm Pharmacol*. 2002;54:1351-1356.
18. Dettmar PW, Sykes J, Little SL, Bryan J. Rapid onset of effect of sodium alginate on gastro-oesophageal reflux compared with ranitidine and omeprazole, and relationship between symptoms and reflux episodes *Int J Clin Pract*. 2006;60:275-283.
19. Reimer C, Lødrup AB, Smith G, Wilkinson J, Bytzer P. Randomised clinical trial: alginate (Gaviscon Advance) vs. placebo as add-on therapy in reflux patients with inadequate response to a once daily proton pump inhibitor. *Aliment Pharmacol Ther*. 2016;43:899-909.
20. Curcic J, Schwizer A, Kaufman E, et al. Effect of baclofen on the mechanism of reflux protection in healthy volunteers and patients with gastro-esophageal reflux disease (GERD) assessed by magnetic resonance imaging (mri) and high resolution manometry (hrm): a randomized controlled study. *Gastroenterology*. 2012;142:S-92-S-93.
21. Sweis R, Kaufman E, Anggiansah A, et al. Post-prandial reflux suppression by a raft-forming alginate (Gaviscon Advance) compared to a simple antacid documented by magnetic resonance imaging and pH-impedance monitoring: mechanistic assessment in healthy volunteers and randomised, controlled, double-blind study in reflux patients. *Aliment Pharmacol Ther*. 2013;37:1093-1102.
22. Kwiatek MA, Roman S, Fareeduddin A, Pandolfino JE, Kahrilas PJ. An alginate-antacid formulation (Gaviscon Double Action Liquid) can eliminate or displace the postprandial 'acid pocket' in symptomatic GERD patients. *Aliment Pharmacol Ther*. 2011;34:59-66.
23. De Ruigh A, Roman S, Chen J, Pandolfino JE, Kahrilas PJ. Gaviscon Double Action Liquid (antacid & alginate) is more effective than antacid in controlling post-prandial oesophageal acid exposure in GERD patients: a double-blind crossover study. *Aliment Pharmacol Ther*. 2014;40:531-537.
24. Meteerattanapipat P, Phupong V. Efficacy of alginate-based reflux suppressant and magnesium-aluminium antacid gel for treatment of heartburn in pregnancy: a randomized double-blind controlled trial. *Sci Rep*. 2017;7:44830.
25. Woodland P, Batista-Lima F, Lee C, Preston SL, Dettmar P, Sifrim D. Topical protection of human esophageal mucosal integrity. *Am J Physiol Gastrointest Liver Physiol*. 2015;308:G975-980.
26. Woodland P, Shen Ooi JL, Grassi F, et al. Superficial esophageal mucosal afferent nerves may contribute to reflux hypersensitivity in nonerosive reflux disease. *Gastroenterology*. 2017;153:1230-1239.

How to cite this article: Deraman MA, Abdul Hafidz MI, Lawenko RM, et al. Randomised clinical trial: the effectiveness of Gaviscon Advance vs non-alginate antacid in suppression of acid pocket and post-prandial reflux in obese individuals after late-night supper. *Aliment Pharmacol Ther*. 2020;51:1014–1021. https://doi.org/10.1111/apt.15746