

Uninvestigated dyspepsia in Brunei Darussalam

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Abstract

Dyspepsia is a common gastrointestinal complaint both in the primary care and hospital settings. It is defined as an abdominal discomfort that is centered in the upper abdomen. This can be attributed to disorders such as peptic ulcer disease, reflux disease, dysmotility disorders, pancreatic disorders, biliary disorders and malignant processes. Functional or non-ulcer dyspepsia accounts for the majority of the cases. Dyspepsia can be categorized into uninvestigated and investigated dyspepsia depending on whether previous evaluations, particularly endoscopy had been carried out. In theory, the management of dyspepsia is straight forward with exclusion of precipitants, use of anti-secretory agents, pro-kinetics or antacids. However, this can be quite difficult for some cases requiring further evaluations and referral to tertiary referral centre. Warning symptoms and family history are important features in deciding when to initiate investigations. Use of over the counter non-steroid anti-inflammatory drugs or salicylate based medications for minor ailments are increasing and should be enquired into, as they are becoming one of the major causes of non-*Helicobacter pylori* (*H. pylori*) related ulcer disease. This article highlights the management of uninvestigated dyspepsia in the setting outside of the hospital environments and proposed a simple management algorithm.

Keywords: endoscopy, functional dyspepsia, uninvestigated dyspepsia, management

1. Introduction

Dyspepsia is a commonly encountered gastrointestinal complaint both in the primary care and hospital settings. It utilizes a significant proportion of the health care resources. Dyspepsia is defined as an abdominal discomfort that is centered in the upper abdomen [1-3]. Definitions of dyspepsia vary between different guidelines. In the guidelines published by the British Gastroenterology Society and the Canadian Dyspepsia Working Group, dyspepsia included 'ulcer-like', 'reflux-like' and 'dysmotility-like' dyspeptic symptoms [4, 5]. The American Gastroenterology Association guideline and the Rome II Consensus exclude 'reflux-like' dyspeptic symptoms as part of dyspepsia and categorized it under gastro-oesophageal reflux disorders [3, 6].

Generally, symptoms arising from the stomach, lower oesophagus, biliary tract, liver and pancreas may be described as dyspepsia. Functional or non-ulcer dyspepsia is a chronic relapsing condition, accounting for upto 60% of patients with dyspepsia [6], and is a major cause of absenteeism [7]. Management begins with a thorough history to localize the possible causes. Warning symptoms and family history of malignancies are important in deciding when to initiate investigations. Use of anti-secretory, antacids, pro-kinetics, eradication of *Helicobacter pylori* infection and avoidance of precipitating agents such as non steroidal anti-inflammatory drugs (NSAIDs) is currently the standard practice [4-5, 8].

2. Prevalence of dyspepsia

2.1 World perspectives

Dyspepsia is a common complaint for consultation, representing 5% of all primary care physician visits [9]. The estimated prevalence rate of uninvestigated dyspepsia ranges from 10-40% with less than half seeking medical care [10]. A phone interview study done in Hong Kong,

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showed that the prevalence of uninvestigated dyspepsia was 18.4% [11]. In the Southeast Asian region, a study done in Singapore showed that uninvestigated dyspepsia was much lower, with an overall prevalence rate of 7.9% [12]. Chinese to have a slightly higher prevalence of 8.1% compared to the Malays (7.3%) and the Indians (7.5%). This difference may represent a real difference in prevalence, as it is widely recognised that the cultural background may influence presentation and health seeking behavior.

2.2 Negara Brunei Darussalam perspective

Dyspepsia has been referred to as ‘oorri’, ‘dugal’, ‘indigestion’ or ‘gastric’ in the local setting. The prevalence of uninvestigated dyspepsia among the general public based on a questionnaire study done locally was 16.8%, being higher among females than males. It is also higher in patients with underlying chronic disorders such as end-stage renal failure patients undergoing regular hemodialysis (34.9%) and rheumatology patients (48%) [13,14]. The overall prevalence of gastrointestinal symptoms in the general populations is shown in Table 1. Dyspepsia represents the leading indications for upper gastrointestinal endoscopy at 59.6 % in our institution, in agreement with published data [5, 15].

Table 1. Prevalence of gastrointestinal symptoms among the public in Brunei Darussalam

<i>Symptoms</i>	<i>Prevalence</i>
Nausea	10.6%
Vomiting	1.5%
Dysphagia	0.3%
Odynophagia	1.2%
Heartburn	8.7%
Early satiety	13.5%
Dyspepsia	16.8%
Abdominal bloating	11.4%

Questionnaire study (n=506)

3. Causes of dyspepsia

The causes of dyspepsia can be divided into organic (structural) and non-organic. For majority of the patients (60%), the underlying cause is often not found despite extensive investigations and such patients are often labeled as suffering from non-ulcer dyspepsia or functional dyspepsia [5]. This is best defined by the Rome II Consensus for functional gastrointestinal disorders, Table 2 [3]. The organic causes include peptic ulcer diseases (*H. pylori* or non-*H. pylori* related), malignant processes of the upper digestive tracts and disorders of the lower oesophagus, biliary tract, pancreas and liver. The pathophysiology of non-ulcer dyspepsia remains poorly defined, however sensory and motor disorders of the stomach and duodenum appear to have a major role in at least a subset of patients [16, 17]. It is important to consider and assess for the presence additional gastrointestinal symptoms as overlapping and clustering are reported to be common, particularly in those with functional dyspepsia [18-21].

Table 2. Rome II Criteria for non-ulcer or functional dyspepsia (1999)

At least 12 weeks, this need not be consecutive, within the preceding 12 months of:

- Persistent or recurrent dyspepsia (pain or discomfort centered in the upper abdomen); and
- No evidence of organic disease (including at upper endoscopy) that is likely to explain symptoms; and
- No evidence that dyspepsia is exclusively relieved by defecation or associated with the onset of a change in stool frequency or stool form (i.e. not irritable bowel syndrome).

In Brunei Darussalam, patients who were evaluated for dyspepsia in the year 2003, 71.3% had normal findings or gastritis/duodenitis on endoscopy, representing the subset that probably had functional or non-ulcer dyspepsia. Reflux disease was seen in 19.3% and peptic ulcer disease in 12.8%. Not surprisingly, the underlying causes of dyspepsia are often the main drive to the current management strategies [5, 22].

4. Management of dyspepsia

4.1 Uninvestigated Dyspepsia

The current management strategies include prompt endoscopy, the 'test and treat' strategy for *H. pylori* and trial of empiric anti-secretory therapy [23]. Due to the complex interplay of the numerous causes, there is currently no single treatment approach that provides a constant and consistent relief of the dyspeptic symptoms.

Patients with alarming symptoms should undergo prompt endoscopy in addition to initiating empiric therapy. A list of such danger symptoms is shown in Table 3. Endoscopy is usually performed without sedation and this is well accepted in our local setting [24]. The issue regarding when to refer for endoscopy has been a matter of debate. Lowering the age of consideration will increase the referral rate and health care cost, making this very unattractive and not cost-effective. This is particularly true in countries where cost of investigations represent major issues. The age consideration needs to be taken into account especially in countries with high gastric cancer rate. Hence, certain cases need to be evaluated on a case by case basis depending on the clinical presentations, risk factors such as strong family history of bowel cancers and warning symptoms.

Table 3. Danger symptoms that should prompt immediate evaluation

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- symptoms onset at age > 45 years old *
 - weight loss,
 - recurrent vomiting,
 - dysphagia,
 - gastrointestinal bleeding,
 - anaemia,
 - family history of gastric cancer,
 - abnormal findings on clinical examinations, and
 - persistence of symptoms despite appropriate therapies
-

*Variable depending on other risk factors and history of malignancy

The presence of additional overlapping or clustering of symptoms should be managed accordingly depending on the nature of these symptoms. Additional investigations such as colonoscopy and radiological imaging of the pancreatico-hepatobiliary system may need to be carried out.

4.2 General measures and advice

Often dyspepsia is associated with irregular meals and consumptions of food that may predispose to onset of symptoms (such as heartburn with sour food). Types of food or lifestyle habits that may predispose to or lead to a worsening of dyspepsia are listed in Table 4. Modifications of eating habits and avoidance of certain food or medications may help relieve symptoms without ever needing any medications. Often these symptoms resolve spontaneously when the precipitants are avoided. Use of over the counter medications such as NSAIDs, salicylate based medications, traditional medications or even medications prescribed from other clinics, should always be enquired. A questionnaire study showed that the local prevalence rate of complementary and alternative medication (CAM) usage among the public was 21.1%. Therefore, it is important to inquire into CAM use as these may account for some of the symptoms [25]. Although many medications can lead to gastrointestinal disturbances, some are more common inducers than others. A list of commonly used medications that may cause dyspepsia is shown in Table 5.

Table 4. Lifestyles and dietary habits that predispose or worsen dyspepsia

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- Irregular dietary habit and unhealthy dietary habit (i.e. over indulgence)
 - Consumption of food that cause intolerance; spicy, oily, lactose, curry, fatty, etc.
 - Smoking
 - Alcohol
 - Coffee
 - Sedentary lifestyle
-

Importantly, thorough explanation and reassurances need to be given, particularly for those with non ulcer dyspepsia. This will also avoid any further unnecessary investigations.

4.3 Complementary and alternative medicine

Use of CAM is widely practiced by patients and it is important to enquire what have been taken as they may be the cause of patients' complaints [26]. This is similarly true in our local setting where CAM is used for all kind of ailments either on their own or supplementary to prescribed medications [25]. Complementary medications can also be

taken to treat dyspepsia, however data on their efficacy is lacking. A systematic review of available studies on alternative medicines has shown that peppermint and caraway have some effects on dyspepsia [27]. No comments can be made regarding the available CAM use for the management of gastrointestinal disorders in our local settings as there is no study to date that has scientifically assessed their use.

Table 5. Medications that are associated with dyspepsia

Over the counter (OTC) medications

• OTC analgesia	NSAIDs
• Salicylate based medicine	Kaki Tiga (Medicinal Powder), Kaki Tiga (Headache Powder), Tooprin, Three Rifles Medicated Powder, Kangda 800.

Prescribed medications

• Anti-platelets	Aspirin
• Cardiac medications	Digoxin
• Respiratory medications	Theophylline
• Antibiotics	Tetracycline, Doxycycline, Erythromycin
• Analgesics	
• NSAIDs	Naproxen (Naproxyn), Naproxen Sodium (Synflex), Ibuprofen, Diclofenac (Voltaren), Indomethacin, Ketoprofen (Oruvail), Sulindac
• Others	Bisphosphonate, Potassium supplement, Iron tablets

Traditional medications

- Traditional medications particularly those taken for musculoskeletal aches
 - Jamu
 - Traditional Chinese medications
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4. 4 Pharmacotherapy

4.4.1 Antacids

Use of antacids such as magnesium hydroxide, aluminum hydroxide, and calcium carbonate are widely practiced either prescribed or self-medicated. Clinical trials have generally not shown significant benefits from antacids [28, 29]. However, due to their availability, low cost and relatively few side effects, use of antacids will remain as part of the first line of dyspepsia management.

4.4.2 Pro-kinetics

Studies on the use of pro-kinetics have produced mixed results. Pro-kinetics agents have been shown to be more effective than placebo in the management of dyspepsia and comparable to histamine-2-receptors antagonists (H2RA) [29]. However, others have shown no benefit of cisapride over placebo [30, 31]. Pro-kinetics may be useful for the management of 'dysmotility-like' dyspepsia, which manifest with symptoms of nausea, vomiting, bloating and early satiety. Currently the options of pro-kinetics (Domperidone and Metaclopramide) are limited with the withdrawal of cisapride from the market due to the association with fatal arrhythmias.

4.4.3 Anti-secretory medications

Histamine-2-receptor antagonists

H2RA medications are widely used for treatment of dyspepsia and have been shown to be superior to placebo and comparable to pro-kinetics for the treatment of dyspepsia [29, 32]. These agents are effective in the treatment of reflux disease and peptic ulcer diseases [33, 34]. Studies comparing H2RA to proton pump inhibitors have shown mixed results but evidences favour the later particularly, in those with 'ulcer-like' or 'reflux-like' dyspepsia [29, 32, 35-37].

Proton pump inhibitors

Potent acid suppression medications particularly the proton pump inhibitors have been shown to be useful in the management of dyspepsia regardless of the sub division of symptoms. Proton pump inhibitors although costing slightly more, have been shown to be superior to

placebo, pro-kinetics (Cisapride) and H2RA (Ranitidine) [32]. The response rates of complete relief of symptoms after four weeks of therapies were 24%, 4%, 8% and 11% for omeprazole, placebo, cisapride and ranitidine respectively. Similarly, another randomized multi-centre study of patients with 'ulcer-like' and 'reflux-like' dyspepsia showed superior symptoms-relief after four weeks with lansoprazole compared to ranitidine (69% vs. 44%, $p = 0.001$) [38].

4.4.4 Miscellaneous

Use of sensory modulators such as tricyclic antidepressant and the newer selective serotonin reuptake inhibitor (SSRI) have been shown to help in some of these symptoms, particularly the subset with non-ulcer or functional dyspepsia. However, before considering starting such treatment, exclusion of organic causes need to be done and therefore such group of patients needs to be referred to specialized unit. This group of patients represent one that can be quite challenging to manage and may require referral for psychological assessments, counseling and therapy in addition to their usual therapy for dyspepsia.

5. Overview

For many persons, the symptoms of dyspepsia are of short duration and mild and are therefore self-managed without ever consulting a doctor [39]. In the management of dyspepsia, differentiating symptoms subsets as described seem a good and reasonable approach, enabling physician to prescribe the 'appropriate' therapy (anti-secretory alone or with a pro-kinetic agents). However, the presence of multiple terminologies for dyspepsia may lead to confusion and misdiagnosis. Similarly, there is a considerable overlap of symptoms presenting among the patients and the difference subgroups; making this approach unhelpful in a subset of patients [40].

An empiric trial of antacid, anti-secretory (H2RA or proton pump inhibitors) or pro-kinetics is recommended before initiating any investigations particularly in those without warning symptoms. Patients started on a trial of empiric therapy should always be followed up to assess symptoms response, usually 4 to 8 weeks later. Follow-

up within this time period is recommended because it is unlikely that an early (and hence curable) gastric cancer would progress to advanced cancer within one to two months of presentation [5]. Patients whose symptoms persist or improve only slightly should be evaluated further with routine blood tests (full blood count, erythrocyte sedimentation rate and liver function tests), faecal occult blood, ultrasound of the abdomen and upper gastrointestinal study (endoscopy or barium study).

Often, the question of how long to maintain patients on their medications is debated. Currently, there is no recommendation as to duration of treatment. Although, use of anti-secretory therapies with H2RA and proton pump inhibitors have been shown to be safe up to ten years of consumption, it is advisable to stop the medications if symptoms have already settled. Taking acid suppression medications on an as required basis has been recommended to reduce unnecessary consumption and reduce health care cost. However, patients need to be followed up and educated on their condition and treatment regime. Patients who require regular analgesics should try alternatives such as non-NSAIDs analgesics (distalgesics) if possible and the duration of treatment kept to a minimal. Co-prescription of anti-secretory medications is an alternative strategy.

In Brunei Darussalam, the endoscopy unit provides an open access referral for endoscopy in patients who require this investigation. Rapid urease tests for *H. pylori* are routinely done for patients regardless of the indications for endoscopy. *H. pylori* is the main cause of peptic ulcer diseases and is a recognised cause of malignancies such as gastric cancer and mucosa-associated lymphoid tissue 1 (MALT) lymphoma [41, 42]. Eradication of this infection has been shown to reduce peptic ulcer recurrence. Our local prevalence is currently around 25% [15]. The rates are higher among the expatriates and the indigenous groups. Among Bruneian expatriates; the Nepalese have the highest prevalence [15, 43].

Association with non-ulcer or functional dyspepsia is not well established and studies looking at treatment responses of non-ulcer or functional dyspepsia with *H. pylori* eradications have shown mixed results. Generally due to the association of *H. pylori* with significant diseases, it is our policy to give eradication therapy if *H. pylori* is

positive. As the only mean available to detect *H. pylori* in the local setting is with gastric biopsies for rapid urease test or histology, patients need to be referred. Serology for *H. pylori* can be done but require special arrangements. Some private clinics can do these tests (serology and urea breath test) as part of the investigations that are available to them. Positive serology indicates exposure to the organism but not necessary active infections whereas, a positive urea breath-test would indicate active infection. Another alternative method for evaluating the upper gastrointestinal tract is by barium contrast study. However this is only recommended if patients refuse endoscopic evaluations.

Table 6. List of available medications in Brunei Darussalam

Antacids

- Evilene Forte Suspension *, Mucaine Gel, Gaviscon Tablet/Liquid, Hydrogel Tablet *, Bismag, Gelusil Plus, Wiselin, Wiselin Plus, Alucid Suspension Antacid Gel Plus, Cenvite, Actal, Actal plus, Victor Antacid, Wiselin Victor, Fullcon's Antacid, Velat-u Stomach tablet, Sure-lin Stomach tablet

Pro-kinetics

- Domperidone (Motilium)*, Metaclopramide (Maxolon)*

Acid Suppression Medications

Histamine -2- receptors antagonist

- Ranitidine *

Proton pump inhibitor

- Omeprazole, Eesomeprazole (Nexium)**
-

* Medications available in peripheral clinics

** Available on name patient basis in government hospital/ also available in JPMC medical centre

OTC antacids (aluminum, magnesium, calcium carbonate and semithicone based antacids) available in certain shops

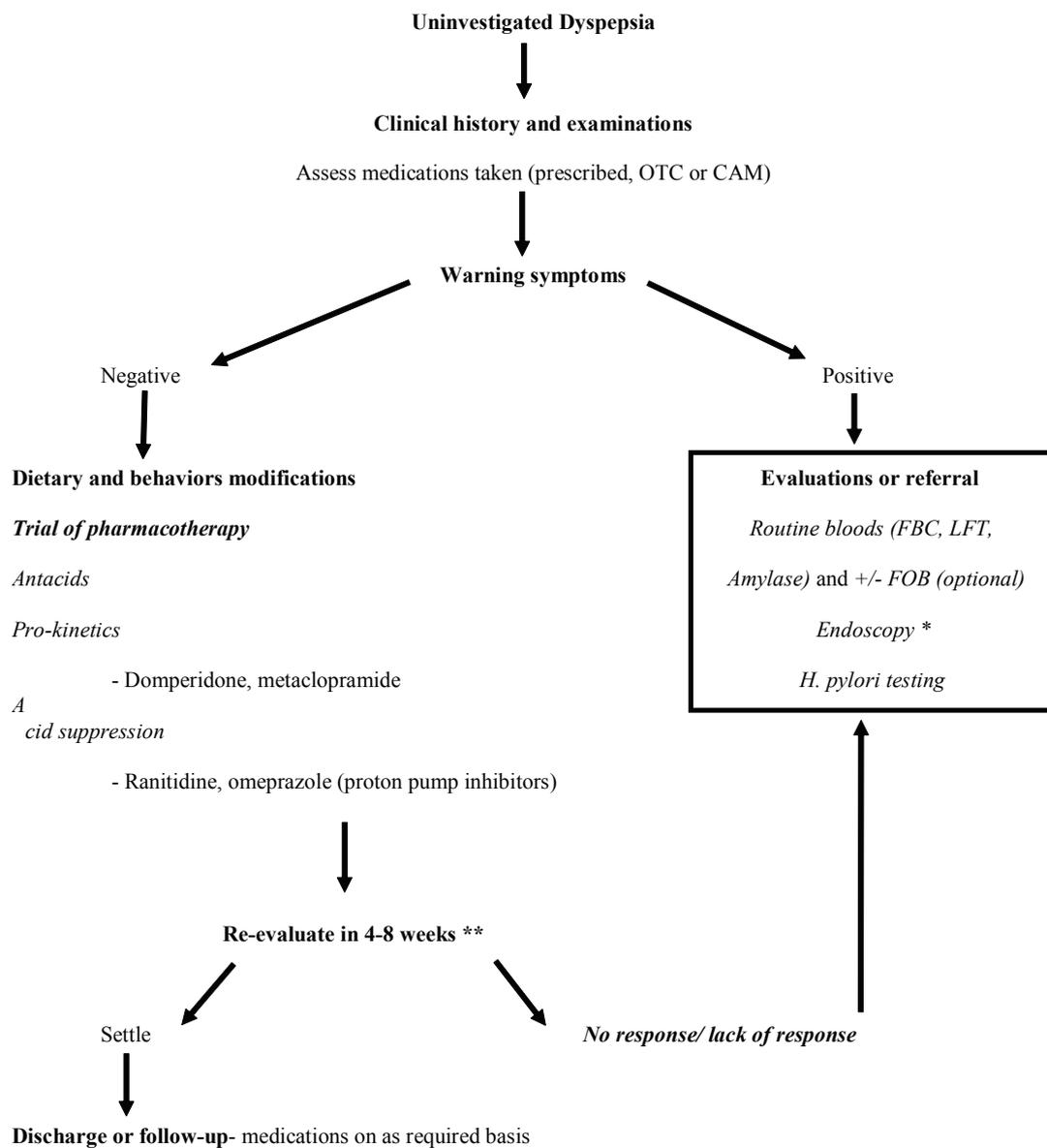
In our local setting, the empirical therapy represents a trial of anti-secretory therapy (H2RA or proton pump inhibitors) with or without antacids. Available medications for treatment of dyspepsia are listed in Table 6.

Prompt referral for endoscopy is always indicated if there are any warning symptoms, no response to empiric

treatment or concern of serious underlying pathologies. A proposed simple algorithm for the management of uninvestigated dyspepsia in the peripheral clinic setting is shown in Figure 1.

In conclusion, uninvestigated dyspepsia remains a problem commonly encountered in our daily practice and

Figure 1. Algorithm for management of uninvestigated dyspepsia



OTC- Over the counter

* Endoscopy represents an important part of evaluation and referral should be prompt if any warning symptoms or failure to response to empirical therapy

** evaluate sooner if there is concern

need to be managed appropriately. Functional or non-ulcer dyspepsia represents the main subset of uninvestigated dyspepsia and their management can be challenging. Empirical therapies are recommended especially for those who do not have any warning symptoms; however they should be monitored for treatment responses. Patient should undergo prompt endoscopy if there is no response to empirical therapies or if there are warning symptoms. It is hope that this review will give guidance to the front line physicians on the management of uninvestigated dyspepsia that they come across in their daily practice.

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