Acupuncture in the Management of Functional Dyspepsia

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ABSTRACT

Dyspepsia is an uncomfortable sensation or pain in the upper abdomen which is persisting or recurring. Dyspepsia can be classified into functional and organic dyspepsia. Functional dyspepsia is more commonly found compared to the organic type, approximately 60%. Pharmacologic therapy in the management of functional dyspepsia has not shown optimal results, with the multifactorial etiology of functional dyspepsia as the main challenge. Therefore, the management of functional dyspepsia is widened and involves variety treatment modalities, acupuncture being one of them. Acupuncture is a way of treatment by puncturing needles to particular area on the skin to eliminate pain and treat particular diseases. Acupuncture affects stomach motility and gastric acid secretion in functional dyspepsia patients. Two acupuncture points commonly used in functional dyspepsia are ST 36 and PC 6. Acupuncture can restore gastric motility in patients with functional dyspepsia, who have gastric emptying disturbance. Besides, functional dyspepsia complaints, such as epigastric pain, nausea, vomiting, anorexia, burning sensation, and bloating were found to improve after acupuncture therapy. Side effects of acupuncture are not life threatening with low incidence rate. The effectiveness of acupuncture therapy compared to standard medication shows varies results. Further studies are needed to determine the characteristics of functional dyspepsia patients which could have optimal results through acupuncture therapy.

Keywords: *epigastric pain, gastric motility, ST 36, PC 6*

ABSTRAK

Dispepsia merupakan rasa tidak nyaman atau nyeri di abdomen bagian atas yang menetap atau berulang. Dispepsia dapat diklasifikasikan menjadi dispepsia fungsional dan organik. Dispepsia fungsional lebih banyak ditemukan daripada tipe organik, yaitu sebesar 60%. Terapi medikamentosa untuk dispepsia fungsional belum menunjukkan hasil optimal. Penyebab dispepsia fungsional yang bersifat multifaktor merupakan tantangan utama. Hal itu menyebabkan tatalaksana dispepsia fungsional meluas dan melibatkan berbagai modalitas terapi, salah satunya adalah akupunktur. Akupunktur adalah suatu cara pengobatan dengan menusukkan jarum pada titik tertentu di kulit untuk menghilangkan nyeri dan mengobati berbagai penyakit tertentu. Akupunktur mempengaruhi motilitas lambung dan sekresi asam lambung pada penderita dispepsia fungsional. Dua titik akupunktur yang umum digunakan pada dispepsia fungsional adalah ST 36 dan PC 6. Akupunktur dapat memperbaiki motilitas lambung pada penderita dispepsia fungsional dengan gangguan pengosongan lambung. Selain itu, keluhan dispepsia fungsional seperti nyeri ulu hati, mual, muntah, anoreksia, rasa terbakar, dan kembung ditemukan berkurang setelah terapi akupunktur. Efek samping akupunktur tidak membahayakan jiwa dengan angka kejadian

yang rendah. Efektivitas terapi akupunktur dibandingkan dengan medikamentosa standar menunjukkan hasil yang bervariasi. Penelitian lebih lanjut diperlukan untuk menentukan karakteristik penderita dispepsia fungsional yang akan mendapat hasil optimal melalui terapi akupunktur.

***Kata kunci**: nyeri ulu hati, motilitas lambung, ST 36, PC 6*

INTRODUCTION

Dyspepsia is defined as uncomfortable sensation or pain in the upper abdomen which is persisting or recurring.[1] This uncomfortable sensation includes a collection of symptoms: nausea, vomiting, early satiation, postprandial fullness, and upper abdominal bloating.[2] The prevalence of dyspepsia in United States ranges between 15-20%.[3] In China and Australia, the prevalence of dyspepsia is 23.5% and 24.4%, respectively.[4]

Dyspepsia is categorized into functional dyspepsia and organic dyspepsia. The etiology of functional dyspepsia is mostly unknown. In contrast, the basic etiology of organic dyspepsia is known. As many as 60% dyspepsia cases are functional dyspepsia.[5] Although functional dyspepsia is not a life threatening disease, 50% functional dyspepsia patients experienced significant decrease in quality of life. Long term medication consumption and obstacles in doing activities during acute exacerbation are the main reasons.[6] Therefore, functional dyspepsia will be further discussed in this review.

Based on Rome III criteria, diagnosis of functional dyspepsia can be established in the presence one or more of these symptoms: postprandial fullness, early satiation, epigastric pain, and burning sensation in the epigastric area, without the presence of organic abnormalities, systemic diseases, or metabolic diseases which could explain the appearance of those symptoms. In addition, those symptoms have been continuing for at least three months and the onset of the first symptom is at least six months before the diagnosis is established.[7]

CLASSIFICATION OF FUNCTIONAL DYSPEPSIA

Functional dyspepsia can be divided into two types based on dominant symptoms felt by the patient, which are epigastric pain syndrome (EPS) and postprandial distress syndrome (PDS).[5] Currently, this classification is mainly used in study because it requires further validation. EPS is defined as moderate to severe degree of pain or burning sensation which is felt intermittently, focused in the epigastrium, and felt at least once a week. Those symptoms do not focused on other area of the abdomen or chest, do not alleviate with defecation or flatulence, and do not fulfill the criteria indicating presence of abnormalities in the bile duct or sphincter of Oddi.

PDS is defined as disturbing postprandial fullness, emerge after normal portion food consumption, and is felt at least several times in a week or early satiety, which cause inability to finish normal portion of food and is experienced at least several times in a week. EPS or PDS symptoms persist for at least three months and the onset of the first symptoms happen at least six months before the diagnosis is established.[5]

Pathophysiology Related to Functional Dyspepsia Symptoms

Functional dyspepsia symptoms are usually associated with digestive process. Almost 60% functional dyspepsia patients experienced symptoms after meal.[8] There are two basic mechanisms proven to play role in the pathophysiology of functional dyspepsia symptoms, such as gastric emptying and gastric accommodation problems.

Gastric emptying in 40% of functional dyspepsia patients occur slower. Slow gastric emptying process could be caused by antrum hypomotility and or duodeno-jejunum dysmotility.[9] Stanghellini et al, stated that this gastric emptying problems played role in the emergence of postprandial fullness, nausea, vomiting, and uncomfortable sensation in the epigastric area, usually experienced by dyspepsia patients.[10]

A study by Tack et al reported that 40% of functional dyspepsia patients had disturbed gastric accommodation (stiff fundus).[11] Optimal gastric accommodation is needed, so that the intra-gastric volume elevation during food digestion process may take place without causing increase in intra-gastric pressure.[12] Presence of gastric accommodation disturbance may lead to the occurrence of early satiety and decrease body weight in functional dyspepsia symptoms.[8] Besides two mechanisms above, psychologic factor also affect the emergence of symptoms in functional dyspepsia patients.[9]

Management of Functional Dyspepsia

One of the approaches in functional dyspepsia management is based on the dominant symptoms found in the patient. In functional dyspepsia with PDS, administration of prokinetic can be considered. This is because gastric emptying problem is assumed to cause PDS. However, it needs to be stressed that the administration of prokinetic will only be beneficial in functional dyspepsia patients with slower gastric emptying. Several functional dyspepsia with PDS patients are found to experience faster gastric emptying, though they experience the similar symptoms. In those patients, administration of prokinetic will not be useful. Administration of cisapride, a prokinetic agent, decrease relative risk of functional dyspepsia patients by 50%.[13]

In functional dyspepsia patients with EPS, administration of anti-depressant may be considered. Through a meta-analysis, Jackson et al, affirmed that anti-depressants were effective to treat functional dyspepsia.[14] However, the effectiveness of anti-depressants in the management of functional dyspepsia is still controversial till date.

Management of functional dyspepsia guidelines by American Gastroenterology Association recommends the administration of proton pump inhibitor for four to eight weeks as first line treatment in patients with functional dyspepsia.[4] This administration of proton pump inhibitor could decrease the relative risk in patients with functional dyspepsia by 30%.[11] In case of no improvement in the symptoms, the administration of prokinetic and anti-depressants could be considered as second line therapy.[4]

Though many approaches in functional dyspepsia management have been developed, the results obtained are controversial. Several studies associated with the use of proton pump inhibitor, prokinetic, and anti-depressants showed inconsistent results. Therefore, till date the optimal management of functional dyspepsia still cannot be determined. The unclear and multifactorial etiology of functional dyspepsia is the main challenge in determining the management. This broadens the functional dyspepsia management, not only through the use of medications, but also acupuncture.

ACUPUNCTURE

The term acupuncture is derived from latin words, *acus* which means needle and *punctura* which means puncture. Acupuncture is a way of treatment by puncturing needles in particular points on the skin to relief pain and treat several health conditions. Though it started as a traditional medicine, today acupuncture has been widely used in the world to treat variable abnormalities.[15]

In line with biomedical development in Western countries, acupuncture has developed into medical acupuncture, which is based on neuroscience and evidence based. WHO has acknowledged acupuncture as a way of treatment and recommend acupuncture to be integrated in national health system.[15]

Acupuncture Mechanism of Action

Based on study, it has been known that acupuncture point is an area on the skin which is different from the surrounding skin tissue as it has higher electrical capacity and potential along with lower electrical resistance. Histologically, there is a structure called neurovascular hemolymphatic complex and denser nerve tissue in acupuncture points. Acupuncture point is a sensitive area that is responsive to inside (diagnostic value) and outside (therapeutic value) stimuli. Stimulation of acupuncture point will activate various specific signal molecules thus influencing many cell functions in the neuro-endocrine-immunologic system to achieve homeostasis condition.[15]

Acupuncture exerts its effects through local, segmental, and central mechanism. In local mechanism, acupuncture produces micro-trauma which cause the release of substance P, calcitonin gene related peptide (CGRP), and β- endorphin. Additionally, acupuncture also stimulates blood coagulation system, immune complex system, afferent somatic and symphatic nerve fibers.[15]

In segmental mechanism, acupuncture stimulates Aδ myelinated (skin) or group III (muscle) small fibers. This stimulation will be delivered to marginal cells in spinal cord and continued through serotonergic (5-HT) fibers to stalk cell. Stalk cell will inhibit gelatinous substance through encephalinergic mechanism to prevent the transmission of pain stimuli.[15]

In central mechanism, acupuncture activates hypothalamus-hypophisis axis which then leads to the release of β-endorphin to the blood and cerebrospinal fluid. This will induce physiologic analgetic and homeostatis of various systems, such as immune, cardiovascular, respiratory, and tissue regeneration. In addition, adrenocorticotropic hormone (ACTH) will stimulate adrenal gland to modify pain sensation, immune reactions, and the secretion of other hormones, such as thyrotropin releasing hormone, growth

hormone, anti diuretic hormone, follicle stimulating hormone, and luteinizing hormone.[15]

Acupuncture and Functional Dyspepsia

The limitation of medicines to improve functional dyspepsia symptoms allows acupuncture to be an option of treatment. In England, 26% functional dyspepsia patients opted acupuncture therapy and 50% of them experienced symptoms improvement.[16]

In regard to functional dyspepsia, symptoms associated with gastrointestinal tract commonly experienced by patients are uncomfortable sensation in epigastric area, nausea, and vomiting. Based on WHO classification, nausea and vomiting have been classified as symptoms which could be effectively treated through acupuncture, based on controlled trials results. Gastric motility problems are classified as condition which has shown acupuncture therapeutic effect, but further studies in this area are still needed.[17]

Acupuncture Mechanism of Action in Improving Functional Dyspepsia Symptoms

Acupuncture mechanism of action in improving functional dyspepsia symptoms involves its affect towards gastroduodenal motility and gastric acid secretion. Two generally used acupuncture points due to its relation with gastroduodenal motility are ST 36 and PC 6.[18]

ST 36 is located on the lower leg and is innervated by sensoric nerve fibers from the fourth lumbar segment of the spinal cord. Stomach is innervated by major splanchnic nerves which is sympathetic from fifth to tenth thoracal segment of the spinal cord. Acupuncture on ST 36 by dermatome, sclerotome, and myotome will cause stimuli to be further delivered to spinal cord up to six segments higher through collateral branches. This puncture will cause stimuli to be further continued to tenth thoracal segment of the spinal cord and later to major splanchnic nerve. Thus, acupuncture on ST 36 may influence gastric motility.[19]

PC 6 is located between tendon musculus palmaris longus and tendon musculus flexor carpi radialis. This point is innervated by sensoric fiber from fifth cervical and first thoracal of the spinal cord. Acupuncture on PC 6 by dermatome, sclerotome, and myotome will be continued to spinal cord up to six segments higher or even reach the brain stem, which is the dorsal location of vagus nerve. Therefore, acupuncture on PC 6 may stimulates vagus nerve, which further affects gastric motility through parasympathetic innervations.[19]

Acupuncture point stimulation may improve gastric motility, both through inhibition or excitation effect. This depends on the location and intensity of the acupuncture point stimulation.[20] Acupuncture stimulation on the stomach will generate inhibition effect towards gastric motility due to excitation of sympathetic innervations through spinal reflex on the lower chest area. Acupuncture stimulation on the extremities will increase gastric motility as a result of excitation of parasympathic innervations through supraspinal reflex.[21] Study performed by Li et al, to 48 adult mice showed that stimulation on LI 11 on the arm and ST 36 on the leg increased gastric motility, while stimulation on ST 21 and CV 6 on the abdomen with the same intensity would decrease gastric motility.[22] A study by Ouyang et al, which was performed to dogs reported that electroacupuncture stimulation on ST 36 and PC 6 would result in shorter gastric emptying duration through the elevation of myoelectrical activity, particularly in the distal gastric area and vagal activity.[23]

Other factor influencing the acupuncture stimulation effect to gastric motility is the stimulation intensity. Li et al, in their study explained that stimulation on any point with the strength below the stimulation threshold of afferent Aδ (group III) fibers would not affect gastric motility effectively.[22] Stimulation with intensity above the stimulation threshold of Aδ (group III) and or C (group IV) was required to influence gastric motility.

Many experts have reported the acupuncture effect towards gastric acid secretion, but the underlying mechanism has not been understood yet. An opinion stated that gastric acid secretion was inhibited through somato-otonom reflex. Some suggested that this mechanism involved endogen opioid.[16] Further studies are needed with regard to acupuncture mechanism of action towards gastric acid secretion.

Study on acupuncture effect to nausea has been done by Tatewaki et al.[18] In that study, 7 dogs which were induced to have nausea by intravenous vasopressin. Those dogs were given acupuncture therapy by giving electrostimulation on PC 6, ST 36, and BL 21. Stimulating PC 6 gave significant improvement in vomiting episodes, while stimulating ST 36 and BL 21 did not produce anti-emetic effect. That anti-emetic mechanism was presumed to be obtained through central opioid pathway.

Studies on acupuncture effect on patients with functional dyspepsia have been performed. Xu et al, conducted a study on 19 functional dyspepsia patients with delayed gastric emptying and nine functional

dyspepsia patients with normal gastric emptying.[24] Electroacupuncture was performed by ST 36 and PC 6. Ten of 19 functional dyspepsia patients with delayed gastric emptying showed significantly improved gastric emptying rate after electroacupuncture ($p = 0.007$). Nine functional dyspepsia patients with normal gastric emptying showed dyspepsia symptoms improvement after electroacupuncture ($p < 0.001$).

A study has been carried out in Indonesia by Setiawan to 12 healthy males aged 20-48.[19] This study evaluated the effect of acupuncture on ST 36 and PC 6 towards gastric emptying rate. Every participant consumed eggs which had been marked with Tc-99m colloid sulphur. Gastric emptying rate examination was performed twice, before and after acupuncture, by using imaging study. Study results revealed elevation in gastric emptying rate in all study subjects with gastric emptying rate average of 27.42 ± 27.65 minutes. This result was in accordance with Tc-99m retention examination results which was lower after acupuncture.

Another study performed by Simadibrata on 30 functional dyspepsia patients, who were randomly assigned evenly into two groups.[25] The first group received acupuncture therapy with punctures on ST 36, LI 4, PC 6, CV 12, LR 3, ST 40, SP 6, ST 25, and BL 21. Acupuncture therapy was performed thrice a week with a total of 12 sessions. Second group received sham acupuncture therapy with the same frequency, however acupuncture was performed on one finger lateral or lateroanterior or lateroposterior from the actual acupuncture point (needle only attached). Based on the study, it was found that improvements of functional dyspepsia symptoms (epigastric pain, nausea, vomiting, anorexia, burning sensation, and bloating) was significant in the first group compared to the second group ($p = 0.000$).

Comparison of Acupuncture and Medication Effectiveness towards Symptoms Improvement in Functional Dyspepsia

Zhou et al, conducted a study evaluating the effectiveness of functional dyspepsia treatment using acupuncture in comparison with domperidone.[26] There were 64 participants received acupuncture therapy with puncture on ST 36, while 62 participants received domperidone therapy. Study results showed that in PDS type functional dyspepsia, both groups showed symptoms improvement with no significant difference between both groups. In non-specific type of functional dyspepsia, acupuncture group experienced more symptoms improvement compared to domperidone group with significant difference statistically ($p < 0.05$).

Cittadini et al, carried out a study in 1996-2001 comparing the effectiveness of acupuncture, domperidone, and placebo in 152 chronic idiopathic dyspepsia patients aged 28-62.[27] Randomly 50 dyspepsia patients in the first group received 12 acupuncture session thrice a week. In every acupuncture session, puncture on ST 36, PC 6, and CV 12 were performed for 30 minutes. Fifty dyspepsia patients in the second group received 10 mg domperidone for two months. Fifty two dyspepsia patients in the third group received placebo in the form of sham acupuncture. Sham acupuncture was performed with the same frequency and duration as in the first group, however puncture was performed to the outer meridian acupuncture point. In this study, dyspepsia symptoms improvement was achieved in acupuncture, domperidone, and placebo group by 70% ($p < 0.01$), 72% ($p < 0.01$), and 23.5% ($p > 0.05$), respectively.

Peng et al, performed a study to 40 functional dyspepsia patients. In that study, 40 functional dyspepsia patients were randomly divided into two groups evenly.[28] First group received acupuncture therapy with puncture on ST 36 and PC 6. Acupuncture therapy was performed daily with 30 minutes duration for two weeks. Second group received cisapride 10 mg three times daily for two weeks. Study results showed significant functional dyspepsia symptoms improvements in both groups ($p < 0.05$). Additionally, acupuncture group also experienced improvements in depression and anxiety ($p < 0.05$).

Advantages and Disadvantages of Acupuncture in Functional Dyspepsia Management

Applying acupuncture as a therapy modality, including in functional dyspepsia has advantages and disadvantages. From the safety aspect, the side effects in acupuncture practice are few. The most commonly found side effects are bruising or bleeding, infection, and dermatitis on the puncture area. Nonetheless, the incidence of these side effects was much lower compared to medications or other medical procedures.[29] Prospective survey in England from June 1998 till February 2000 reported that the incidence of minor side effects in acupuncture practice was 671/10,000 acupuncture consultation. The most common side effects were bleeding (310/10,000 consultation) and pain due to puncturing (110/10,000 consultation).[30]

We have not found literature review assessing the cost effectiveness of acupuncture therapy in functional

dyspepsia management. Nevertheless, acupuncture therapy has been proven to be cost-effective in the management of chronic neck pain, chronic cephalgia, and allergic rhinitis.[31,32]

Based on controlled trials results, WHO has stated that nausea and vomiting have been classified as symptoms which have been proven to be treated effectively by acupuncture. Gastric motility problem is classified as conditions for which the therapeutic effect of acupuncture has been shown but for which further proof is needed.[17] However, studies comparing effectiveness of acupuncture therapy and standard medication in functional dyspepsia management showed varying results.

CONCLUSION

Management of functional dyspepsia with medication has not shown consistent results. Presently, acupuncture is a therapy modality which can be considered in functional dyspepsia management. Acupuncture may improve gastric motility in functional dyspepsia patients with gastric emptying problem. In addition, functional dyspepsia complaints, such as epigastric pain, nausea, vomiting, anorexia, burning sensation, and bloating are found to be improved after acupuncture therapy. Side effects of acupuncture usually are not life threatening with low incidence rate. Effectiveness of acupuncture compared to standard medication showed vary results. Thus, further studies are needed to be able to determine the characteristics of functional dyspepsia patients which could obtain optimal results through acupuncture therapy.

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