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Review Article

Effects and underlying mechanisms of acupuncture on functional dyspepsia: a narrative review

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Abstract: Functional dyspepsia (FD) is common among the general population and has a complicated pathogenesis. A number of patients with FD seek complementary therapies as symptom alleviation with conventional treatment is unsatisfactory. Acupuncture, with its 3000-year history in China, has been reported to be helpful in treating functional gastrointestinal disorder. This review discusses the recent research on the effects and mechanisms of acupuncture treatment for FD. Trials suggest that acupuncture may be beneficial in improving the symptoms and quality of life in FD patients. The underlying mechanisms include improving the impaired gastric accommodation to a meal and the delayed gastrointestinal emptying, and reducing hypersensitivity to gastric distension. If the different FD subcategories and the measurement of their clinical outcomes are considered, the true effects of acupuncture will be better revealed.

Keywords: Functional dyspepsia, functional gastrointestinal disorder, acupuncture, complementary, alternative medicine

Introduction

Functional dyspepsia (FD) is characterized by recurrent or long-lasting abdominal pain or discomfort without evidence of organic disease [1]. Pathophysiologic mechanisms, such as impaired gastric accommodation to a meal, delayed gastric emptying, and visceral hypersensitivity to gastric distension, contribute to the complex dyspeptic symptoms of FD [2]. Despite the continuous improvement in the diagnostics and pharmacologic treatment of FD, the outcome is still below expectation [3, 4]. Therefore, a number of patients with FD seek complementary therapies [5].

Acupuncture has a 3000-year history in China. In ancient traditional Chinese medicine (TCM) theory, the human body has an energy force known as qi, the flow of which may affect human health. It is believed that the balance of qi can be restored by acupuncture, thus maintaining well-being [6]. Acupuncture is described as a procedure that stimulates anatomical points of the body, called acupoints, using a solid metallic needle which penetrates the skin. The technique is developed in Eastern countries, and has been used in functional gastrointestinal disorders including FD for a long time [7]. The exact mechanism by which acupuncture affects FD is not understood. In this article, we reviewed the recent studies on acupuncture treatment of FD to explore its effects and underlying mechanisms.

Therapeutic effects of acupuncture on FD

A report published in 2017 analyzed 7 trials with 542 participants and discussed the efficacy of acupuncture in FD [8]. In four trials, acupuncture was compared with common drugs used in FD treatment, and the results demonstrated no significant differences [9]. Both acupuncture and drugs improved the symptoms of the patients [10]. However, acupuncture had fewer adverse effects than the drugs [11]. Three trials which compared acupuncture to sham acupuncture found that acupuncture had

a better outcome during the treatment and follow-up periods [12]. Acupuncture significantly improved symptoms including abdominal fullness after meals, and the sensations of pressure, cramps, and burning in upper abdomen [13].

It is important to realize that patient with FD have, in addition to a stomach disorder requiring treatment, a state of disharmony induced by specific psychosocial situations [9]. The quality of life (QOL) is affected among patients with FD when compared to the general population [10]. The Short-form 36-items Health Survey Quality of Life (SF-36) and Nepean Dyspepsia Life Quality Index (NDLQI) are commonly used to measure the health-related QOL of FD patients. Several studies supported the benefit of acupuncture to the QOL of FD patients, which was demonstrated by the SF-36 [11] and NDLQI measurements [12].

Potential mechanisms of acupuncture in FD

Effects of acupuncture on digestive dysmotility

Delayed gastric emptying has been reported in 20%-50% of patients with FD [13]. Acupuncture could up-regulate electrogastrographic frequencies and promote gastric emptying in patients with FD. The gastric emptying of solids was also accelerated with electric acupuncture (EA) at Zusanli (ST36) and Neiguan (PC6) [14].

Many patients with FD have impaired accommodation in the proximal stomach. The accommodation reflex is regulated by the vagus nerve. EA restored impaired gastric accommodation induced by vagotomy in a canine model [15]. EA at ST36 improved gastric dysrhythmia and impaired accommodation, both of which seemed to be mediated mainly by the vagal pathway [16]. It was considered that acupuncture at ST36 enhanced vagal activity, potentiating the impaired accommodation reflex among FD patients [17].

Visceral hypersensitivity has been considered a pathophysiological mechanism in functional gastrointestinal disorders since the 1980s [18]. FD patients have an increased intragastric perception of mechanical stimuli. EA at ST36 relieved gastric distension-induced gastralgia in rats [19]. In addition, transcutaneous electrical nerve stimulation (TENS) raised the discomfort threshold to gastric distension [20].

Effects of acupuncture on brain-gut interaction

Neuroimaging studies showed that acupuncture might modulate the widely distributed cortical and subcortical brain areas. There are a series of studies which aimed at exploring the effect of acupuncture on brain activities among FD patients. The results showed that compared to the controls, in FD patients, glycometabolism was reduced at the cingulated gyrus, the left caudate tail, and the right orbital gyrus, while it was increased at the left inferior temporal gyrus. After acupuncture at *Liangqiu* (ST34), ST36, *Fenglong* (ST40), and *Chongyang* (ST42), glycometabolism was decreased at the cerebellum, and postcentral gyrus, and enhanced at the vision-related cortices. It was suggested that the caudate tail, prefrontal cortex, and anterior cingulate cortex were related to processing gastric perception in FD patients. The deactivation of the cerebellum and primary somatosensory area was caused by acupuncture stimulation [21].

The neuroimaging data indicated that patients with FD showed more deactivation in the brain after acupuncture at the acupoints ST34, ST36, ST40, and ST42. The deactivated areas included the brainstem, anterior cingulate cortex (ACC), insula, thalamus, and hypothalamus, whereas, only deactivations of the brainstem and thalamus were found after acupuncture at non-acupoints. Thus, the ACC, hypothalamus, and insula, which regulate the homeostatic afferent network, might be related to the specific mechanism of acupuncture.

Effects of acupuncture on metabolic profile

Compared to healthy individuals, FD patients had lower levels of total lipids, N-acetyl glycoprotein (NAc), leucine/isoleucine, and lactate, and higher levels of phosphatidylcholine (PtdCho), glucose, and acetate. Higher levels of glucose and lower levels of total lipids and lactate in FD patients suggested the glycolytic rate was reduced, and energy consumption had shifted to lipid oxidation. Acupuncture appeared to reduce these changes to some extent and demonstrated efficacy in relieving functional dyspepsia symptoms. In addition, EA could also decrease low-density lipoprotein/very low-density (LDL/VLDL) and increase NAc levels, altered by FD in tail-clamped rats. This may explain the improvement in the symptoms of FD patients.

Discussion

Functional dyspepsia is common in the general population and its pathogenesis remains unclarified [22]. Clinical trials indicate that acupuncture might be beneficial in improving symptoms and QOL in FD patients [23-25]. However, as FD is a heterogeneous disorder with nonspecific symptoms and a diverse pathophysiology, it is difficult to find an effective therapy for FD patients. In a recent systematic review, a definitive conclusion relating to the efficacy of acupuncture in FD was not found [12]. This might be because the different subcategories of FD patients were ignored. It is a problem that all the patients are assumed to be pathophysiologically similar, are grouped into one large heterogeneous category, and receive the same acupuncture treatment. Rome III criteria subcategorizes FD into postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). PDS is meal-related, and is featured by early satiation and postprandial fullness. EPS is meal-unrelated, and is featured by epigastric burning and pain [26, 27]. This means that the dyspeptic symptoms of some FD patients are aggravated by food ingestion while the others are not. This difference might reflect the different pathogenesis between the EPS and PDS patients, and may be used for developing targeted therapy [28, 29]. Further research might divide patients into subgroups requiring different acupuncture modalities. The specific effects of acupuncture for FD might, then, be shown better.

Acupuncture is a therapeutic method based on the TCM classification of syndromes [30]. Patients are evaluated by both western medicine and TCM methods [31]. The acupoints are selected according to the TCM diagnosis, the physician's personal experience, and the localization of pain or symptom modalities [32, 33]. A study, aimed at checking the effects of acupuncture, provides some relevant information on acupoint selection. It suggested that acupuncture based on the TCM classification of syndromes is more effective for migraine than acupuncture at basic acupoints [34, 35]. However, acupoint selection has been skipped in the studies of FD, apart from one Chinese trial that check the effects of acupuncture based on the TCM classification of syndromes [36, 37]. The FD patients who received acupuncture at basic acupoints and additional acupoints after TCM classification of syndromes had better gastrointestinal function and improved dyspeptic symptoms than patients who received acupuncture at only basic acupoints. Therefore, appropriate acupoint selection remains essential for its effect. If the TCM classification of syndromes is used in acupuncture trials of FD, its outcome will be more credible and its true effects will be better revealed. It will improve our understanding of FD pathophysiology, and provide researchers and physicians with better protocols to treat FD.

Although FD is a chronic disease which does not severely affect the long-term health of individuals, the patients' QOL dramatically reduces. SF-36 and NDLQI are usually employed to assess the efficacy of therapeutic interventions. It appears that SF-36 does not identify the special aspects of QOL influenced by some diseases as generic instruments [38, 39]. Whereas, NDLQI is a disease-specific instrument which can assess QOL from five perspectives: drinking and eating, daily life, sleep and tension, study and jobs, and control and knowledge [40, 41]. In NDLQI, patients not only report their QOL in each area, but also point out the importance of each, This weightage for importance is added in each area, the area with greater relevance to the overall QOL getting a higher score. As many measures of QOL like SF-36 and NDLQI are available, the risk of their inappropriate usage may be increased. Three more questions need to be asked. First, how many changes in QOL scores are clinically significant? Second, how can be their specificity be evaluated? Third, how can the suitable method be chosen?

The most commonly used acupoints in treating patients with FD include ST36, *Zhongwan* (CV12), PC6, ST40, and ST34 in the clinical trials. Acupuncture is performed to treat patients with FD three to five times a week over a 4-week period. The long-term efficiency and relapse after acupuncture deserves to be observed. Additionally, although patients with FD usually have psychological problems and poor QOL, studies have paid less attention to them. In order to understand the psychological morbidities of FD better, the relationship between acupuncture treatment and psychological problems needs further investigation.

Conclusion

We reviewed recent research suggesting the effects and underlying mechanisms of acu-

puncture treatment in FD. Some randomized controlled trials which aim to investigate the effects of acupuncture on FD patients are going on [42, 43]. They will help us understand the therapeutic potential of acupuncture in FD. It is expected that the use of acupuncture together with the current therapies will be more widespread and frequent in the treatment of FD patients.

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Disclosure of conflict of interest

None.

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References

[1] Carbone F, Holvoet L, Vanuytsel T, Tack J. Rome III functional dyspepsia symptoms classification: severity vs frequency. Neurogastroenterol Motil 2017; 29.

[2] Zhou J, Li S, Wang Y, Lei Y, Foreman RD, Yin J, Chen JD. Effects and mechanisms of auricular electroacupuncture on gastric hypersensitivity in a rodent model of functional dyspepsia. PLoS One 2017; 12: e0174568.

[3] Camilleri M, Stanghellini V. Current management strategies and emerging treatments for functional dyspepsia. Nat Rev Gastroenterol Hepatol 2013; 10: 187-194.

[4] Talley NJ, Weaver AL, Zinsmeister AR. Impact of functional dyspepsia on quality of life. Dig Dis Sci 1995; 40: 584-589.

[5] Lima FA, Ferreira LE, Pace FH. Acupuncture effectiveness as a complementary therapy in functional dyspepsia patients. Arq Gastroenterol 2013; 50: 202-207.

[6] Wang F, Qin Y, Li L, Li M. Correlation between spirit-qi acupuncture and lifting-thrusting twirling method for spirit in Huangdi Neijing. Zhongguo Zhen Jiu 2016; 36: 274-278.

[7] Li H, He T, Xu Q, Li Z, Liu Y, Li F, Yang BF, Liu CZ. Acupuncture and regulation of gastrointestinal function. World J Gastroenterol 2015; 21: 8304-8313.

[8] Lan L, Zeng F, Liu GJ, Ying L, Wu X, Liu LM. Acupuncture for functional dyspepsia. Cochrane Database Syst Rev 2014; 13: CD008487.

[9] Enck P, Azpiroz F, Boeckxstaens G, Elsenbruch S, Feinle-Bisset C, Holtmann G, Lackner JM, Ronkainen J, Schemann M, Stengel A. Functional dyspepsia. Nat Rev Dis Primers 2017; 3: 17081.

[10] Rich G, Shah A, Koloski N, Funk P, Stracke B, Köhler S, Holtmann G. A randomized placebo-controlled trial on the effects of Menthacarin, a proprietary peppermint-and caraway-oil-preparation, on symptoms and quality of life in patients with functional dyspepsia. Neurogastroenterol Motil 2017; 29.

[11] Lv L, Wang FY, Ma XX, Li ZH, Huang SP, Shi ZH, Ji HJ, Bian LQ, Zhang BH, Chen T. Efficacy and safety of Xiangsha Liujunzi granules for functional dyspepsia: a multi-center randomized double-blind placebo-controlled clinical study. World J Gastroenterol 2017; 23: 5589-5601.

[12] Pang B, Jiang T, Du YH, Li J, Li B, Hu YC, Cai QH. Acupuncture for functional dyspepsia: what strength does it have? A systematic review and meta-analysis of randomized controlled trials. Evid Based Complement Alternat Med 2016; 2016: 3862916.

[13] Asano T, Aida S, Suemasu S, Tahara K, Tanaka KI, Mizushima T. Aldioxa improves delayed gastric emptying and impaired gastric compliance, pathophysiologic mechanisms of functional dyspepsia. Sci Rep 2015; 5: 17519.

[14] Xu S, Hou X, Zha H, Gao Z, Zhang Y, Chen J. Electroacupuncture accelerates solid gastric emptying and improves dyspeptic symptoms in patients with functional dyspepsia. Dig Dis Sci 2006; 51: 2154-2159.

[15] Huang Z, Zhang N, Xu F, Yin J, Dai N, Chen JD. Ameliorating effect of transcutaneous electroacupuncture on impaired gastric accommodation induced by cold meal in healthy subjects. J Gastroenterol Hepatol 2016; 31: 561-566.

[16] Sarosiek I, Song G, Sun Y, Sandoval H, Sands S, Chen J, McCallum RW. Central and peripheral effects of transcutaneous acupuncture treatment for nausea in patients with diabetic gastroparesis. J Neurogastroenterol Motil 2017; 23: 245-253.

[17] Jin H, Liu J, Foreman RD, Chen JD, Yin J. Electrical neuromodulation at acupoint ST36 normalizes impaired colonic motility induced by rectal distension in dogs. Am J Physiol Gastrointest Liver Physiol 2015; 309: G368-G376.

[18] Simrén M, Törnblom H, Palsson OS, van Tilburg MA, Van Oudenhove L, Tack J, Whitehead WE. Visceral hypersensitivity is associated with GI symptom severity in functional GI disorders: consistent findings from five different patient cohorts. Gut 2018; 67: 255-262.

[19] Lin Y, Peng Y, Yi S, Tang S. Effect of different frequency electroacupuncture on the expres-

sion of substance P and beta-endorphin in the hypothalamus in rats with gastric distension-induced pain. Zhen Ci Yan Jiu 2009; 34: 252-257.
[20] Coffin B, Azpiroz F, Guarner F, Malagelada JR. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. Gastroenterology 1994; 107: 1345-1351.
[21] Lee IS, Wang H, Chae Y, Preissl H, Enck P. Functional neuroimaging studies in functional dyspepsia patients: a systematic review. Neurogastroenterol Motil 2016; 28: 793-805.
[22] Talley NJ. Moving away from focussing on gastric pathophysiology in functional dyspepsia: new insights and therapeutic implications. Am J Gastroenterol 2017; 112: 141-144.
[23] Liu Z, Tang Z, Tian J. Targeting mechanisms of typical indications of acupuncture. In: editors. multi-modality neuroimaging study on neurobiological mechanisms of acupuncture. Springer 2018; 61-89.
[24] Ho RST, Chung VCH, Wong CHL, Wu JCY, Wong SYS, Wu IXY. Acupuncture and related therapies used as add-on or alternative to prokinetics for functional dyspepsia: overview of systematic reviews and network meta-analysis. Sci Rep 2017; 7: 10320.
[25] Chiarioni G, Pesce M, Fantin A, Sarnelli G. Complementary and alternative treatment in functional dyspepsia. United European Gastroenterol J 2018; 6: 5-12.
[26] Walker MM, Andreasson A, Falkeis C, Vieth M, Talley NJ, Agreus L. Tu1208 Prevalence of Antral Gastritis in the General Population in Subjects With Rome III Functional Dyspepsia, Epigastric Pain Syndrome (EPS) and Post Prandial Distress Syndrome (PDS). Gastroenterology 2015; 148: S-822.
[27] Drossman DA, Hasler WL. Rome IV-functional GI disorders: disorders of gut-brain interaction. Gastroenterology 2016; 150: 1257-1261.
[28] Holtmann G, Rich G, Wieland V, Funk P, Kieser M, Koehler S. Menthacarin for the treatment of epigastric pain syndrome (EPS) and postprandial distress syndrome (PDS): data of a placebo-controlled trial revisited. Zeitschrift für Gastroenterologie 2015; 53: KG253.
[29] Bisschops R, Karamanolis G, Arts J, Caenepeel P, Verbeke K, Janssens J, Tack J. Relationship between symptoms and ingestion of a meal in functional dyspepsia. Gut 2008; 57: 1495-1503.
[30] O'Connor J, Bensky D. Acupuncture: a comprehensive text. Editora Roca 1981.
[31] Yue P, Xuelin D, Tiejian Z, Le Y, Yanfei W, Guiyu L. Construction of rat model of hepatic fibrosis with blood stasis syndrome integrated with traditional chinese medicine (TCM) syndrome and western medicine disease. Animal Husbandry and Feed Science 2017; 9: 101-107.
[32] Melchart D, Linde K, Streng A, Reitmayr S, Hoppe A, Brinkhaus B, Becker-Witt C, Wagenpfeil S, Pfaffenrath V, Hammes M, Willich SN, Weidenhammer W. Acupuncture Randomized Trials (ART) in patients with migraine or tension-type headache-design and protocols. Forsch Komplementarmed Klass Naturheilkd 2003; 10: 179-184.
[33] Linde K, Streng A, Jürgens S, Hoppe A, Brinkhaus B, Witt C, Wagenpfeil S, Pfaffenrath V, Hammes MG and Weidenhammer W, Willich SN, Melchart D. Acupuncture for patients with migraine: a randomized controlled trial. JAMA 2005; 293: 2118-2125.
[34] Facco E, Liguori A, Petti F, Zanette G, Coluzzi F, De Nardin M, Mattia C. Traditional acupuncture in migraine: a controlled, randomized study. Headache 2008; 48: 398-407.
[35] Da Silva AN. Acupuncture for migraine prevention. Headache 2015; 55: 470-473.
[36] Ma C, Huang Q, Wan W, Zhou L, Tang L, Wang Y, Luo Q, Zhang T, Wang Y. Effects of syndrome-differentiation acupuncture on life quality in patients with functional dyspepsia. Zhongguo Zhen Jiu 2014; 34: 125-129.
[37] Yang Y, Ai F, Ma CY, Wan WJ, Li HY. Observation on clinical therapeutic effect of acupuncture treatment on functional dyspepsia based on syndrome differentiation. Zhongguo Zhong Xi Yi Jie He Za Zhi 2015; 35: 411-414.
[38] Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Med Care 1992; 30: 473-483.
[39] Nantes SG, Strand V, Su J, Touma Z. Comparison of the sensitivity to change of the 36-item short form health survey and the lupus quality of life measure using various definitions of minimum clinically important differences in patients with active systemic lupus erythematosus. Arthritis Care Res (Hoboken) 2018; 70: 125-133.
[40] Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. Ann Intern Med 1993; 118: 622-629.
[41] Naito M, Suzukamo Y, Fujii W, Seta H, Murata K, Naito T, Kikutani T. Quality of life and perspectives of happiness in middle-aged and older people with dysphagia. Value Health 2015; 18: A427.
[42] Han G, Ko SJ, Park JW, Kim J, Yeo I, Lee H, Kim SY and Lee H. Acupuncture for functional dyspepsia: study protocol for a two-center, randomized controlled trial. Trials 2014; 15: A427.
[43] Zheng H, Xu J, Li J, Li X, Zhao L, Chang X, Liu M, Gong B, Li X, Liang F. Acupuncture for patients with functional dyspepsia: study protocol of a randomised controlled trial. BMJ Open 2013; 3: e003377.