



BENSON-HENRY INSTITUTE
FOR MIND BODY MEDICINE
AT MASSACHUSETTS GENERAL HOSPITAL



Non-Pharmacologic (and non-surgical) Approaches for GERD Management

Michelle Dossett, MD, PhD, MPH
mdossett@mgh.harvard.edu

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Disclosures

- I have no relevant financial conflicts of interest
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Outline

- Acupuncture
- Mind-Body Approaches
- Dietary Supplements
- Lifestyle Interventions
- Patient-Clinician Interaction
- Summary

Why Non-Pharmacologic Approaches?

- Although PPIs are very effective for reducing acid production, not all patients have a satisfactory response
- Chronic PPI use is associated with multiple potential adverse effects
- Many patients do not like taking daily medications

Acupuncture

Clinical Study on the Treatment of Gastroesophageal Reflux by Acupuncture

ZHANG Chao-xian (张超贤)¹, QIN Yong-mei (秦咏梅)¹, and GUO Bao-rui (郭宝瑞)²

Group	Case	Time	Times of reflux with pH < 4	
			Total	Long-term
Treatment	30	T0	83.17 ± 73.68	10.46 ± 3.43
		T1	36.15 ± 42.16*	4.68 ± 5.84*
		T2	39.78 ± 22.59	5.45 ± 3.37
Control	30	T0	82.52 ± 56.24	10.53 ± 4.09
		T1	35.63 ± 47.69*	4.72 ± 4.87*
		T2	49.47 ± 35.53 [△]	6.26 ± 5.03 [△]

* $P < 0.01$, compared with T0 in the same group; [△] $P < 0.05$, compared with T1 in the same group;

Treatment: acupuncture daily with 2-3 day breaks each week x 6 weeks

Control: omeprazole 20mg BID + mosapride 20 mg TID x 6 weeks

T0 = baseline,

T1 = after 6 weeks of treatment

T2 = 4 weeks after cessation of treatment

Clinical trial: acupuncture vs. doubling the proton pump inhibitor dose in refractory heartburn

R. DICKMAN^{*,†}, E. SCHIFF^{‡,§}, A. HOLLAND^{‡,¶}, C. WRIGHT[¶], S. R. SARELA^{*}, B. HAN^{*} & R. FASS^{*}

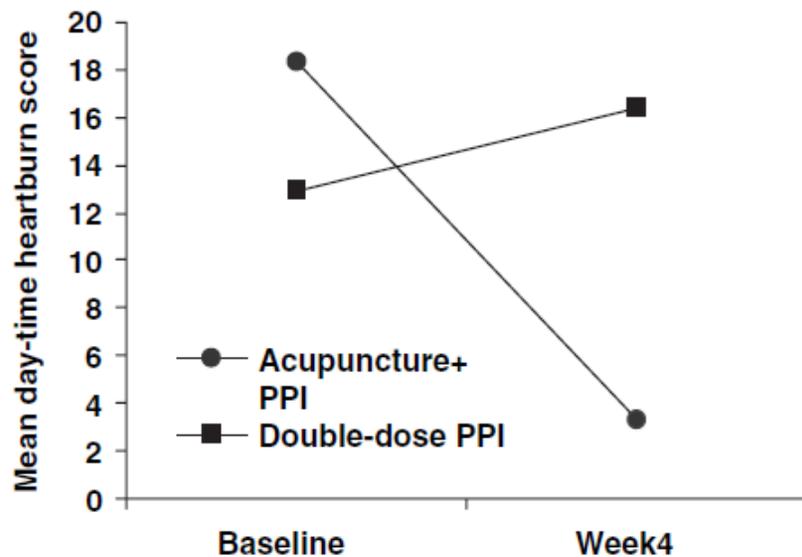


Figure 2. Comparison of mean day-time heartburn score between the two patient groups (within groups comparison – for acupuncture + PPI – $P < 0.001$; for double-dose PPI $P = NS$; between groups comparison – $P < 0.001$).

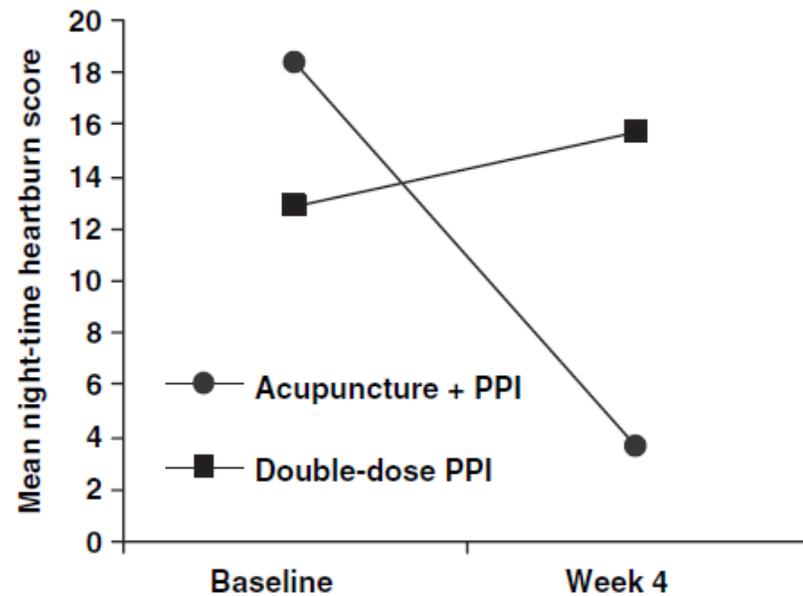
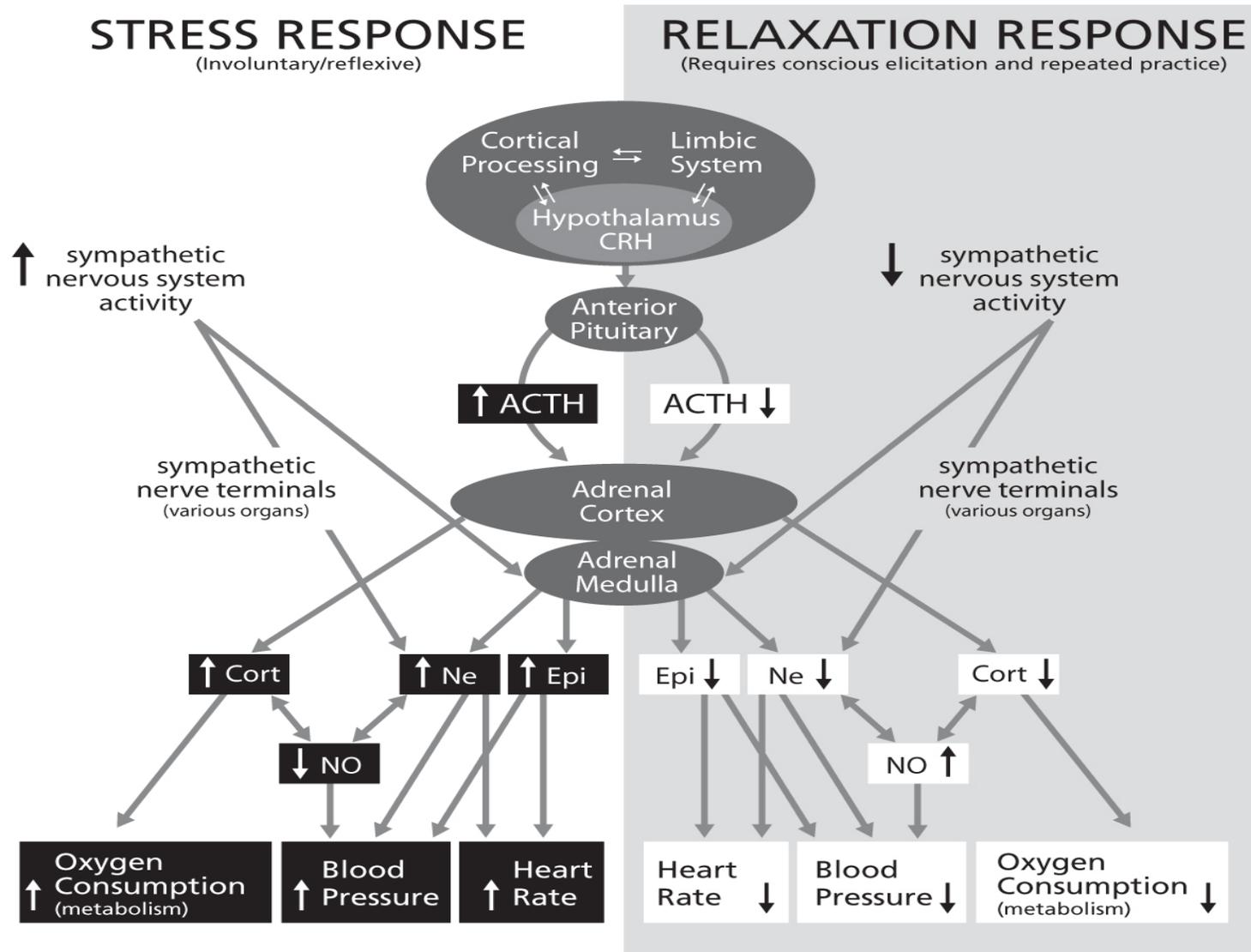


Figure 3. Mean night-time heartburn score between the two patient groups (within groups comparison: for acupuncture + PPI – $P < 0.001$; for double-dose PPI $P = NS$; between groups comparison – $P < 0.001$).

Mind-Body Medicine

- Practices that focus on the interactions among the brain, mind, body, and behavior, with the intent to use the mind to affect physical functioning and promote health.
- Includes: meditation, deep-breathing exercises, guided imagery, progressive muscle relaxation, biofeedback, yoga, qi gong, and tai chi.

Physiologic Changes with Mind-Body Practices



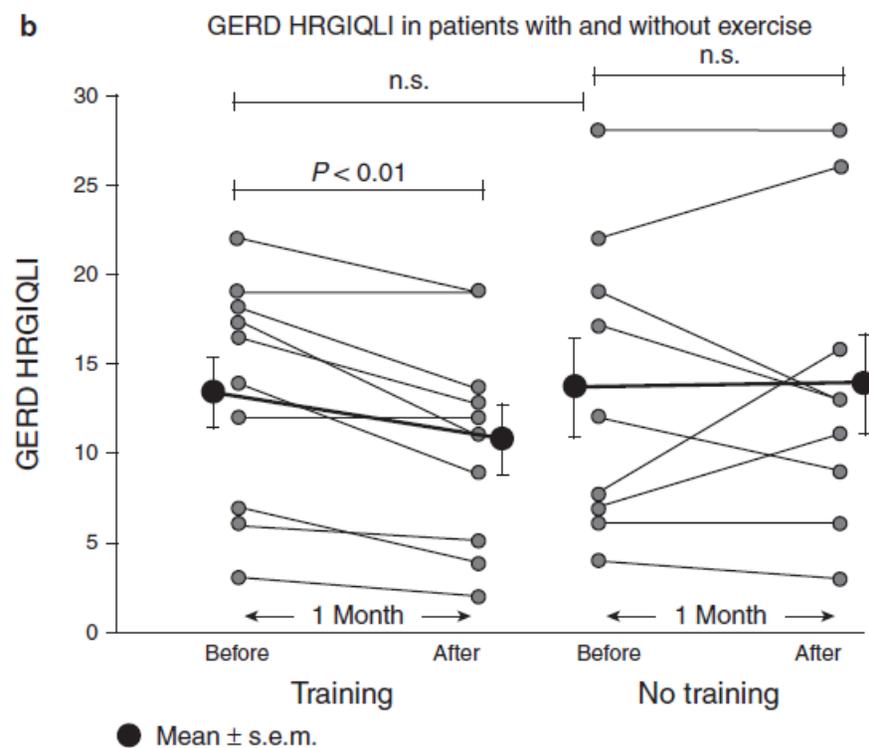
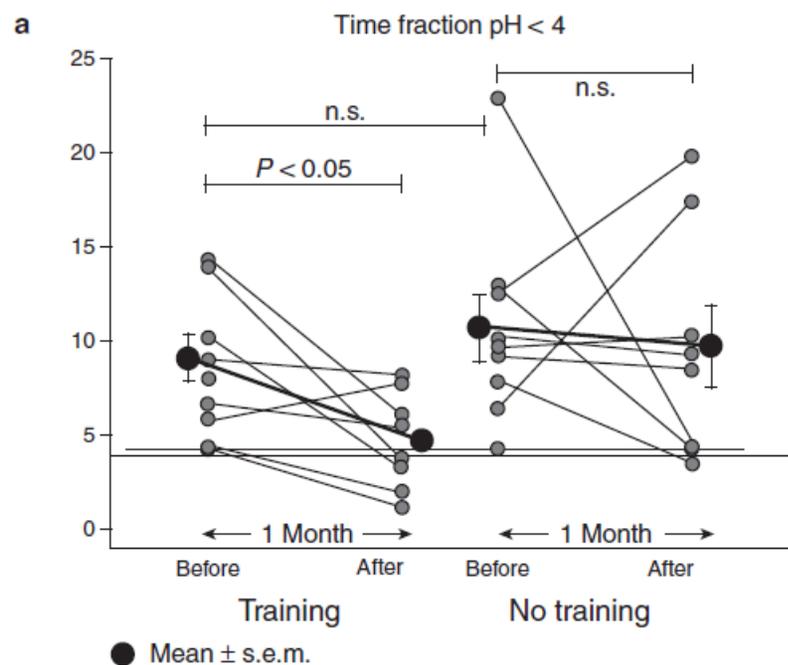
GERD & Mind-Body Approaches

- Stress increases the perception of GERD symptoms.
- Several reports have suggested that mind-body therapies such as hypnotherapy, biofeedback, and progressive muscle relaxation can reduce GERD symptom severity.

Mizyed, Aliment Pharmacol Ther 2009; Gordon, J Clin Gastroenterol 1983; Shay, J Clin Gastroenterol 1986; Colgan, Lancet 1988; McDonald-Haile, Gastroenterology 1994.

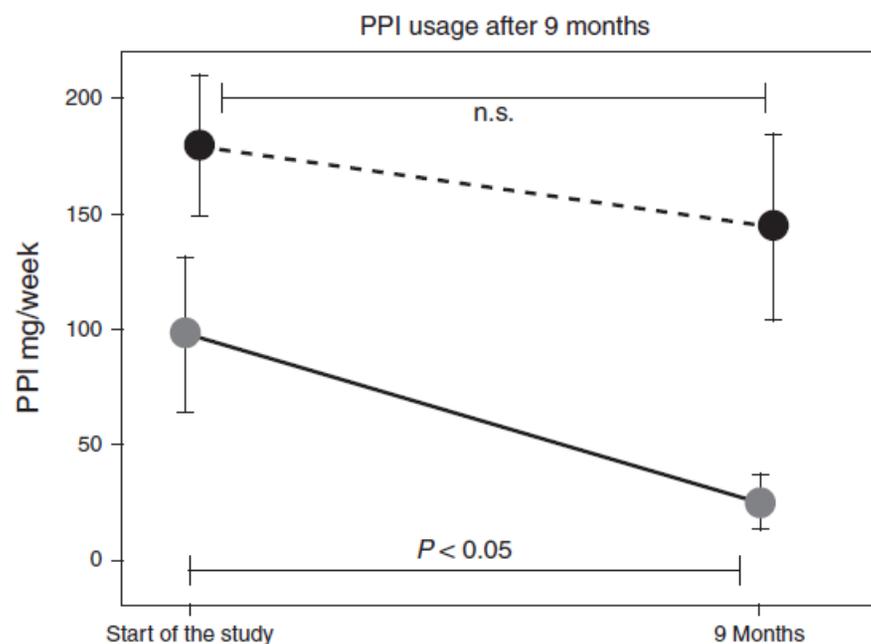
Positive Effect of Abdominal Breathing Exercise on Gastroesophageal Reflux Disease: A Randomized, Controlled Study

A.J. Eherer, MD¹, F. Netolitzky¹, C. Högenauer, MD¹, G. Puschnig¹, T.A. Hinterleitner, MD¹, S. Scheidl, MD², W. Kraxner, MD¹, G.J. Krejs, MD¹ and Karl Martin Hoffmann, PD, MD³



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Meditation & Mindfulness?

- No reported studies in the literature for GERD.
- Several studies reporting benefits for sleep*.
- At BHI, many patients state that stress worsens their GERD symptoms & that these symptoms improve when they participate in our mind-body program.
- Same for sleep.
- Possible mechanism?

*Ong, *Sleep*, 2014; Black, *Jama Intern Med*, 2015.

Association of Acute Gastroesophageal Reflux Disease With Esophageal Histologic Changes

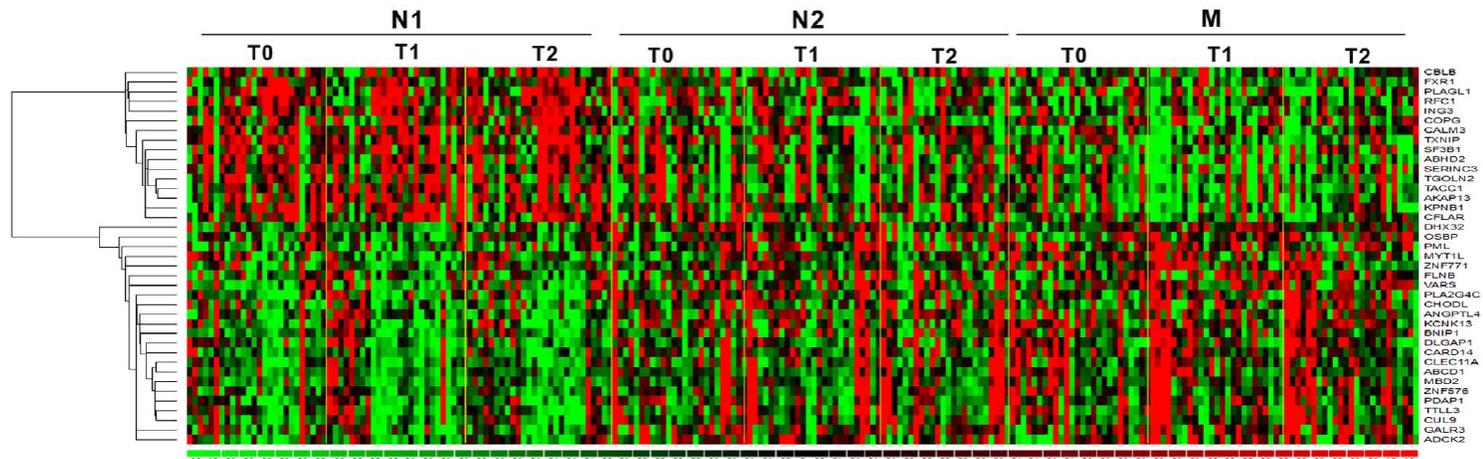
Kerry B. Dunbar, MD, PhD; Agoston T. Agoston, MD, PhD; Robert D. Odze, MD; Xiaofang Huo, MD, PhD; Thai H. Pham, MD; Daisha J. Cipher, PhD; Donald O. Castell, MD; Robert M. Genta, MD; Rhonda F. Souza, MD; Stuart J. Spechler, MD

Histologic Finding ^a	Baseline (With PPIs), Median (Range)	Week 1 (Without PPIs), Median (Range)	P Value	Week 2 Without PPIs, Median (Range)	P Value
Intraepithelial					
Lymphocytes	0 (0 to 2)	1 (1 to 2)	.005	1 (1 to 2)	.002
Neutrophils	0 (0)	0 (0 to 2)	.32	0 (0 to 2)	.18
Eosinophils	0 (0 to 1)	0 (0 to 1)	.32	0 (0 to 1)	.32
Basal cell and papillary hyperplasia	0.5 (0 to 1)	2 (1 to 3)	.002	2 (1 to 3)	.003
Spongiosis (dilated intercellular spaces)	0.5 (0 to 1)	2 (1 to 3)	<.001	2 (1 to 3)	<.001

Cessation of PPI therapy was associated with T cell lymphocyte infiltration, widening of intracellular spaces, and basal cell hyperplasia without loss of surface cells, suggesting that reflux esophagitis may be mediated by cytokine rather than acid-related injury.

Changes in Gene Expression with Meditation Practice over 8 weeks

- > 1500 differentially regulated genes including decreases in inflammatory pathways (esp NF- κ B) and increased nitric oxide production



Dusek, *PLoS ONE*, 2008
Bhasin, *PLoS ONE*, 2013

Dietary Supplements

RESEARCH ARTICLE

Open Access

The potential therapeutic effect of melatonin in gastro-esophageal reflux disease

Tharwat S Kandil^{1*}, Amany A Mousa², Ahmed A El-Gendy³, Amr M Abbas³

	Melatonin	Omeprazole	Melatonin and Omeprazole	P value		
D) Melatonin level at day time (pg/ml):				P1	P2	P3
control	36.1 ± 2.3	36.1 ± 2.3	36.1 ± 2.3	1.0	1.0	1.0
pretreatment:	18.2 ± 5.54	18.5 ± 3.75	18.3 ± 3.8	0.1	0.665	0.472
4 weeks	28.26 ± 2.26	19.2 ± 3.47	28.83 ± 1.82	0.000	0.55	0.000
8 weeks	34.5 ± .35	17.9 ± 3.72	34.5 ± 2.35	0.000	1.00	0.000

RESEARCH ARTICLE

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	Melatonin	Omeprazole	Melatonin and Omeprazole	P value		
				P1	P2	P3
1-LES pressure(mmHg)						
control	22.8 ± 1.3	22.8 ± 1.3	22.8 ± 1.3	0.9	0.9	0.9
pretreatment:	10 ± 1.58	10.5 ± 2.86	10.3 ± 1.68	0.65	0.7	0.86
4 weeks	14.5 ± 1.58	10.4 ± 4.05	14.5 ± 1.26	0.006	0.468	0.002
8 weeks	20.2 ± 1.56	10.5 ± 2.85	20.5 ± 1.22	0.000	0.68	0.000
C) PH (at 5 cm above the LES):						
control:	7.8 ± 0.4	7.8 ± 0.4	7.8 ± 0.4	1.0	1.0	1.0
pretreatment:	2.3 ± 0.36	2.1 ± 0.38	1.98 ± 0.37	0.1	0.1	0.1
4 weeks	5.2 ± 0.5	5.9 ± 0.48	6.1 ± 0.55	0.008	0.002	0.09
8 weeks	6.7 ± 0.65	7.2 ± 0.32	7.5 ± 0.31	0.01	0.008	0.1
D) BAO(mmol/h)						
- control:	2.6 ± 0.6	2.6 ± 0.6	2.6 ± 0.6	1.0	1.0	1.0
pretreatment:	24.7 ± 0.5	25.1 ± 0.6	24.9 ± 0.7	0.1	0.1	0.1
4 weeks	20.1 ± 0.4	17.2 ± 0.7	15.8 ± 0.9	0.008	0.002	0.09
- 8 weeks	16.6 ± 0.6	11.5 ± 0.6	10.2 ± 0.9	0.01	0.008	0.1

Regression of gastroesophageal reflux disease symptoms using dietary supplementation with melatonin, vitamins and aminoacids: comparison with omeprazole

Ricardo de Souza Pereira

Table 2. Healing rates of patients in the two treatment groups

	Group A (<i>n</i> = 176)	Group B (<i>n</i> = 175)	<i>P</i> -value	χ^2 -test
PP analysis (%)	176/176 (100)	115/173 (66.5)	0.001	70.766
ITT analysis (%)	176/176 (100)	115/175 (65.7)	0.001	72.785

Group A: Melatonin (6 mg), tryptophan (200 mg), vitamin B12 (50 μ g), methionine (100 mg), vitamin B6 (25 mg), betaine (100 mg) and folic acid (10 mg).

Group B: Omeprazole 20 mg/day

Meta-analysis: phytotherapy of functional dyspepsia with the herbal drug preparation STW 5 (Iberogast)

J. MELZER*, W. RÖSCH†, J. REICHLING‡, R. BRIGNOLI§ & R. SALLER*

*Department of Internal Medicine, Complementary Medicine, University Hospital Zurich, Zurich, Switzerland;

†Medical Clinic, Hospital Nordwest, Frankfurt on Main, Germany; ‡Institute of Pharmacy and Molecular Biotechnology, University of Heidelberg, Heidelberg, Germany; §Tradysen GmbH, Rüslikon, Switzerland

Table 1. Composition of STW 5

Drugs extracted

(ethanolic 30%, DER 1:3)

Angelicae radix (Garden angelica root)

Cardui mariae fructus (Milk thistle fruits)

Carvi fructus (Caraway fruits)

Chelidonii herba (Greater celandine)

*Iberis amara** (Bitter candy tuft)

Liquiritiae radix (Liquorice root)

Matricariae flos (Chamomile flowers)

Melissae folium (Balm leaves)

Menthae piperitae folium

(Peppermint leaves)

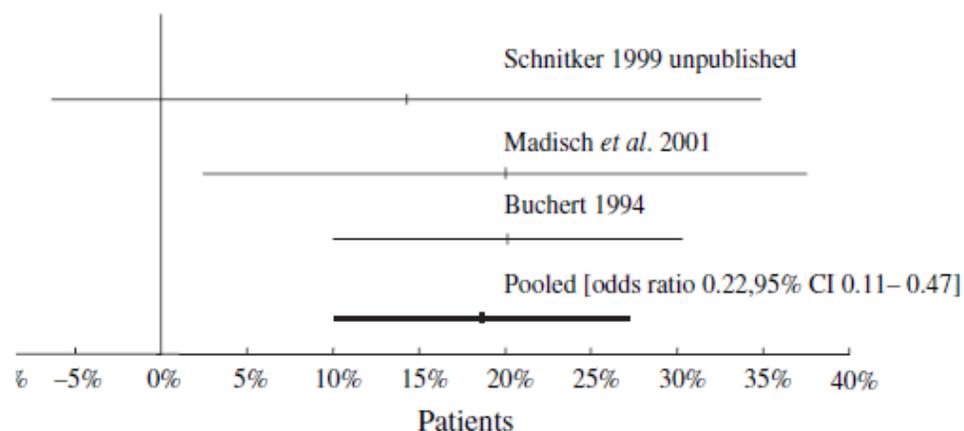


Figure 2. Rate difference between assessments of the most bothersome symptom with STW 5 and with placebo treatment and 95% CI (19% more patients with reduction from very severe/severe to mild/absent in the STW 5 group).

Raft agents

- Alginate and pectin (and synthetic derivatives)
- Rise to the top of the gastric contents and form a physical barrier protecting mucosa and blocking reflux of acidic contents into the esophagus.

Other Supplements

- Betaine HCl or apple cider vinegar
- Deglycyrrhizinated licorice (DGL)
- Chamomile
- Slippery elm
- Marshmallow root
- D-limonene

Used by some, but there are few if any RCTs.

Note – mint can exacerbate symptoms due to LES relaxation.

Lifestyle Approaches

- In a large review only weight loss and elevation of the head of the bed were consistently associated with improvement in GERD symptoms.
- Dietary triggers and/or a large evening meal may also play a role for some individuals.

Therapeutic Effects of the Clinical Relationship

- The patient-provider relationship affects health outcomes across a range of health conditions.
- Complementary and integrative medicine provider visits may have enhanced patient-provider relationship effects.
- Many patients with gastrointestinal conditions seek out complementary therapies.

Patient-Provider Interactions Affect Symptoms in Gastroesophageal Reflux Disease: A Pilot Randomized, Double-Blind, Placebo-Controlled Trial

Michelle L. Dossett^{1*}, Lin Mu^{1,2}, Roger B. Davis^{1,3}, Iris R. Bell⁴, Anthony J. Lembo⁵, Ted J. Kaptchuk^{1,6}, Gloria Y. Yeh¹

	Acidil	Placebo
Standard Visit	n=6	n=6
Expanded Visit	n=6	n=6

Sample Expanded Interview Questions

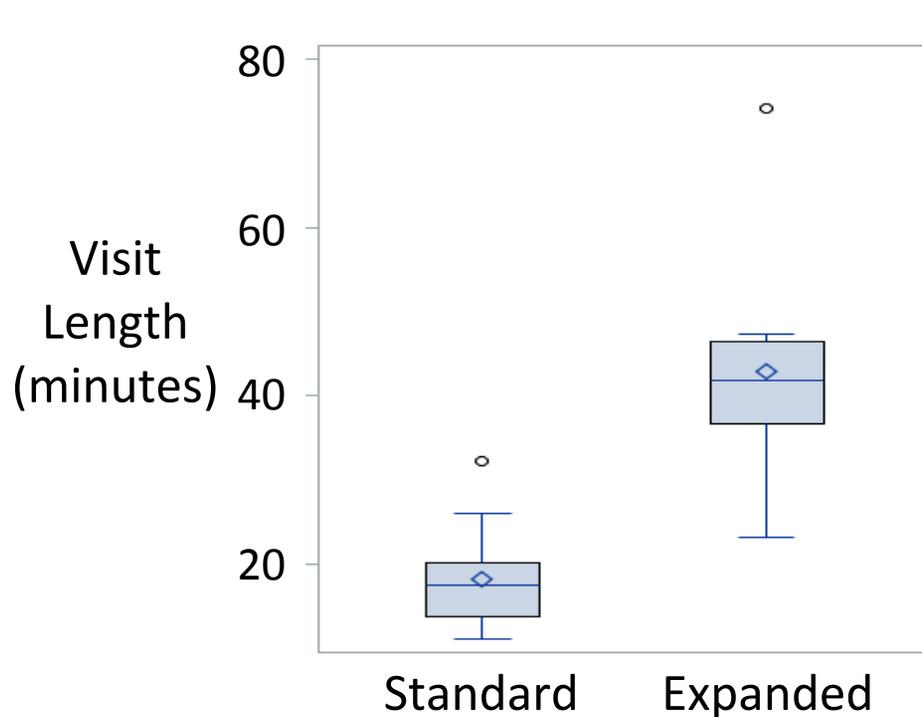
- Does the time of day or weather affect the severity of your symptoms?
- Tell me about your appetite and the foods that you crave and that you cannot stand.
- How is your body temperature? Do you prefer to be warmer or cooler? Effect of temperature on energy?
- Do you have any fears or phobias?

Primary and Secondary Outcomes

Analysis	Standard vs. Expanded	Placebo vs. Acidil
≥ 50% improvement in GERD severity (primary)	p = 0.01*	p = 0.33
GERD severity	p = 0.01*	p = 0.20
Dyspepsia severity	p = 0.01*	p = 0.66
GERD-HRQL score	p = 0.08	p = 0.09

* significant at $p < 0.05$

What Mediated These Improvements... Visit Length?

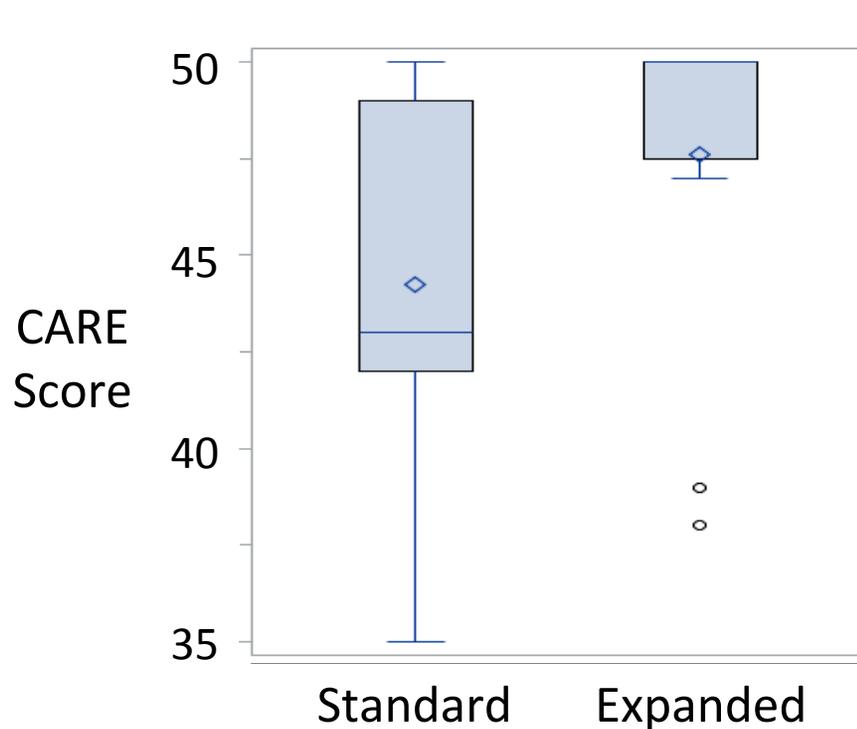


	<u>Median</u>	<u>Range</u>
Standard	18	11-32
Expanded	42	23-74

$p = 0.0005$

When added to the ANCOVA model to test for association with treatment outcomes, $p = 0.50$

What Mediated These Improvements... Perceived Empathy?



	<u>Median</u>	<u>Range</u>
Standard	43	35-50
Expanded	50	38-50

$p = 0.09$

When added to the ANCOVA model to test for association with treatment outcomes, $p = 0.44$

Potential Mechanisms

More than just time – how the time is spent matters

- Being heard in a safe and non-judgmental space may function as a form of interpersonal healing / narrative medicine
- Unique questions may prompt self-reflection and change patients' perceptions of their illness
- May elicit a physiologic response similar to meditation in which patients feel at ease and are receptive – enhancing awareness while improving coping and adherence.

Summary

- There is good evidence for acupuncture, raft-forming agents, weight loss, and elevating the head of the bed for reducing GERD-related symptoms.
- There is reasonable evidence to consider mind-body approaches (especially if stress may be playing a role), melatonin, Iberogast, and dietary modification (in patients who notice an association).
- An enhanced patient-clinician interaction may also have a therapeutic effect.

Acidil®

- Homeopathic product marketed for heartburn symptoms
- Combination of 4 homeopathic medicines
 - Abies nigra 4C
 - Carbo vegetabilis 4C
 - Nux vomica 4C
 - Robinia pseudoacacia 4C
- 4C = 10^{-8} dilution



Table 2: Mean baseline and follow-up symptom severity and quality of life scores (standard deviation) and between group comparisons.

Characteristic*	P / Std (n=6)	A / Std (n=6)	P / Exp (n=6)	A / Exp (n=6)	Std vs. Exp [^]	P vs. A [^]
GERD severity						
# of responders	2	0	5	4	p = 0.011	p = 0.33
Baseline	4.2 (2.1)	5.6 (2.6)	3.6 (2.2)	3.8 (2.3)		
Follow-up	2.9 (2.3)	4.2 (2.1)	0.8 (0.8)	1.7 (1.5)	p = 0.012	p = 0.20
Dyspepsia severity						
# of responders	1	1	4	4	p = 0.041	p = 1.00
Baseline	7.2 (5.1)	5.2 (3.7)	6.0 (4.6)	7.2 (2.7)		
Follow-up	5.2 (3.7)	4.3 (2.6)	1.8 (1.6)	3.3 (1.2)	p = 0.013	p = 0.663
GERD-HRQL score						
Baseline	24.5 (7)	27.0 (9)	26.2 (9)	27.5 (2)		
Follow-up	18.2 (5)	26.3 (8)	17.7 (3)	18.3 (5)	p = 0.076	p = 0.092

* Higher numbers signify worse symptoms or worse quality of life.

[^] p values represent main effects from exact logistic or ANCOVA models. Trends favored the expanded and placebo interventions. All standard/expanded visit x Placebo/Acidil treatment interactions were non-significant.