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Evidence-based summaries and critical reviews on the latest developments in integrative therapies [ALERT]

ENERGY MEDICINE

Energy Medicine: Is There Evidence?

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Dr. Selfridge reports no financial relationships relevant to this field of study.

Accepting the possibilities of healing or creating positive effects on human health and disease through deliberate manipulation of putative subtle energies is challenging for many conventionally trained Western health providers. Even though we take advantage of the body's constant generation of electromagnetic energy using diagnostic tools such as the ECG, EEG and MRI, energy discharges so small that they escaped detection until we had tools refined enough to discover them, and we find it harder to accept the idea that some other yet unidentified energetic forces might exist in the human body, might be related to health and disease, and might be subject to intentional manipulation. However, the assumption that such subtle energies exist and can be affected by certain individuals has been a keystone of many cultural healing traditions for millennia. Despite separation by time and distance between many of these cultures, the energetic concepts supporting the development of energy therapies are remarkably similar. These cultures assume the presence of a life force or energy that permeates all living things. Examples include the Indian "prana," Chinese "chi," and Japanese "qi." This vital force may travel in well-organized and reliable pathways within the human body (e.g., "meridians" in traditional Chinese medicine) and may generate "fields" of energy that can be detected by certain trained or endowed humans (e.g., "auras" described in several spiritual traditions). Interruption or disorganization of this vital force is presumed to underlie physical, mental, and emotional disease and suffering. It is also assumed that perturbations of this vital force can and must be corrected or augmented for healing, optimum health, and well-being.

Interest in subtle energies in the West is a recent phenomenon. Wilhelm Reich, a protégé of Sigmund Freud, emigrated to the United States from Germany in 1939 to conduct and disseminate research on a vital force he claimed to discover called the Orgone. Although his work was controversial and discredited publicly, he had many followers in the United States and internationally who claimed beneficial effects from

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his "Orgone accumulator," including cancer cures.[1]

The U.S. nursing profession began more widely teaching and implementing energy therapies known as healing touch (HT), therapeutic touch (TT), and Reiki (see *Table 1*) in the 1970s in clinical and hospital settings. Nurse academicians have produced much of the limited extant research on these modalities. Patients are actively using energy medicine modalities and may not be informing their physicians. A survey from the National Institute of Health Statistics in 2004 reported that about 1% of respondents had used Reiki or qi gong in the previous year. However, this proportion increased to more than 45% when intercessory prayer and healing ritual were included.[2] Use of energetic therapies is probably underestimated in patient surveys; many practitioners of other therapeutic modalities, such as nurses, massage therapists, and chiropractors, blend energy therapies into their work without labeling these therapies as such.

Non-clinical experiments aimed at exploring possible subtle energy effects challenge one's skepticism. Radin reported temporal EEG correlations in pairs of people isolated in separate locations when one of the pair was stimulated at random times by live video of the other person.[3] This EEG analysis was corroborated by a similar EEG study by Standish in 2004, and a case report using a similar study design showing fMRI correlates under similar circumstances.[4,5] These results were supported by Achterberg et al in an fMRI study of 22 subjects: 11 healers using distant intention paired with 11 recipients. Recipients were studied by fMRI while each healer performed distant intention in random 2-minute intervals for his/her paired recipient, according to preferred healing practice. Significant differences were found between the "send" intervals and the "no send" intervals in the activity of the brains of the recipients ($P = 0.000127$).[6] Uchida et al reported the effects of Okada Purifying Therapy (OPT) on the EEG of subjects. In the OPT group, the subjects sat facing a wall with the therapist positioned behind them without touching or making noise. Subjects were given instruction to open and close their eyes at timed intervals during 15 minutes of intentional therapy. Placebo group subjects were positioned similarly with

Table 1: Descriptions of a Limited List of Energy Medicine Therapies

Name	Description
Healing Touch	Developed in the 1980s by nurse Janet Mentgen, who integrated energetic therapies she was using in her nursing practice. Relies on a detailed understanding of energy centers and meridian and involves light touch. Requires extensive training for certification.
Therapeutic Touch	Developed in the 1970s by nurse Delores Krieger and Dora Kunz. Gentle touch is used to manipulate the biofield.
Reiki	A Japanese energy intervention founded by Japanese Buddhist monk Mikao Usui in the 1920s. Uses prescriptive hand positions, and healing ability is passed on during training during an "attunement" provided by a Reiki master.
Johre	Founded by Mokichi Okada in the 1930s, it involves channeling light energy to recipients through the hands of the therapist without involving touch.
Qi gong	An ancient, traditional Chinese energy therapy balances chi using movement, breath entrainment, and mental/meditation training.
Polarity Therapy	Developed by Randolph Stone, an osteopath, in the early- to mid-20th century, involves gentle touch, prescriptive diet, and exercise to influence vital energies.
Okada Purifying Therapy	Another school of the therapeutic techniques founded by Mokichi Okada focuses on energy channeling through the hands of the therapist to the recipient without touch involved.
Thought Field Therapy	Founded by Roger Callahan and based on traditional Chinese medicine concepts, clients are guided by the therapist to tap on acupoints and meridians in prescriptive sequences for the condition being addressed.

Summary Points

- Several non-clinical experiments suggest the presence of subtle and yet undefined forces that can be directed to others to produce measurable biological effects.
- So far, conclusions about the therapeutic value of energy therapies are hindered by a lack of well-designed research studies. Current limited evidence best supports touch therapies for low-grade reduction of pain intensity.
- Despite insufficient evidence to support clinical guidelines, the safety and accessibility of energy therapies make them viable options as adjunct treatments when patients express a preference for them.

a non-therapist sitting quietly behind them while subject EEGs were similarly monitored and then analyzed. OPT recipients demonstrated a significant increase in alpha wave output during the therapy ($P < 0.05$).[7] Pike et al measured asymmetrical cortical activation during EEG in subjects receiving an energetic therapy called IRECA (Istituto di Ricerca sull'Energia Cosmica Applicata) compared to placebo and no treatment groups.[8] This energetic therapy involves practitioner attentional and intentional focus to transfer energy for the purpose of healing or performance enhancement. Subjects were randomized and blinded to the treatments and had been "stressed" immediately prior to the interventions by completing a cognitively demanding task. Left anterior frontal cortex activation was significantly increased in recipients receiving IRECA compared to placebo ($P = 0.037$) and no treatment ($P = 0.002$). Left anterior frontal cortex activation has been previously reported in meditation studies to be associated with improved immune function, vitality, well-being, and quicker recovery from exposure to negative stress.[8] Abe et al reported increased viability loss in cultured human gastric cancer cells exposed to 72 hours of Johrei treatments compared to cultures of untreated cells.[9] The results of these studies strongly suggest "something is happening," although mechanisms remain elusive. Roe et al performed a meta-analysis of extant research on the effects of intentional energetic therapies on biological systems other than "whole humans," including studies of bacterial and yeast cultures, whole blood, plants, and cell cultures. Studies were rated on a scale of 10 for methodological quality using an adapted version of the SIGN50 tool created by the Scottish Intercollegiate Guidelines Network (average score was 4.3). Forty-nine studies met inclusion criteria and were subjected to the analysis. A significant effect size was noted (r, the correlation coefficient and a standard measure of effect size, was reported as 0.204, indicating better outcomes for the "treatment" groups compared to controls).[10]

ENERGY MEDICINE/BIOFIELD MODALITIES

The National Center for Complementary and Integrative Health labels energetic therapies that manipulate putative subtle energies not yet measurable by available technology as "biofield therapies." Biofield therapy practices include local or proximal practices, wherein the healer guides energy while in the physical presence of the patient, and distance practices, wherein the healer guides energy to the recipient who is in a different physical location. An excellent overview and description of energy medicine is provided by Rindfleisch in *Integrative Medicine*.[11] A limited description of some popular energy medicine interventions covering those modalities that are the focus of this review is provided here in Table 1.

RECENT RESEARCH

A well-constructed systematic review and best evidence synthesis by Jain and Mills reviewed 66 studies of a variety of proximally practiced biofield therapies that met inclusion criteria: 1) published in English in a peer-reviewed journal, and 2) quantitative biological and/or psychological endpoints. Randomized, controlled trials (RCTs) were included (n = 52), as well as within-subject repeated measure designs (n = 14). All studies were assessed and given points for quality parameters of design and methodology, statistical methods, and outcomes. Studies were rated as high or low quality based on median scores, and the mean score for study quality was 6.4 out of 12. From these studies, levels of evidence were assessed for the efficacy of biofield therapies for specific patient populations, conditions, and outcomes:

- **Level 1 – "Strong evidence"** supported by findings from two high-quality RCTs and generally consistent findings in other studies
- **Level 2 – "Moderate evidence"** supported by findings from at least one high-quality RCT and supported by at least one lower-quality RCT or high-quality quasi-experimental study
- **Level 3 – "Limited evidence"** supported by more than one lower-quality quasi-experimental study and/or lower-quality RCT
- **Level 4 – "Conflicting evidence"** supported by multiple studies with conflicting results

In a best-evidence synthesis, it was concluded that there is strong evidence for biofield therapy efficacy for reducing pain intensity and improving quality of life in pain populations, although evidence is equivocal for impact on affective measures associated with pain. Only moderate evidence exists for pain intensity reduction in hospitalized and cancer patients. Moderate evidence exists for decreasing negative behaviors in dementia patients and for decreasing anxiety in hospitalized patients. Only equivocal evidence exists for the other clinical conditions

studied, including anxiety in heart patients and fatigue and quality of life for cancer patients.[12]

Anderson and Taylor focused on HT research in clinical practice for a systematic review.[13] Five studies met their inclusion criteria and these were assessed for quality and assigned a score using modified Jada criteria. Their conclusions about the efficacy of HT were similar: Methodological flaws and limited number of quality studies make inferences about efficacy impossible.

A 2008 Cochrane Review meta-analysis of "touch therapies" for pain relief, including Reiki, HT, and TT, included 24 studies and 1153 participants. Pain intensity was reduced, on average, by 0.83 units on a 1-10 scale in patients treated with touch therapy compared to control patients (95% confidence interval [CI], -1.16 to -0.50). This review noted that effect size appeared greater for Reiki studies and when more experienced practitioners delivered the treatments. In studies that evaluated analgesic use, touch therapies appeared to reduce analgesic use. Placebo effect in these trials was analyzed, and the authors concluded that no statistically significant ($P = 0.29$) placebo effect could be identified.[14]

A 2012 qualitative review of published research on biofield therapies for cancer pain (Anderson and Taylor) written for oncology nurses concluded that evidence of efficacy for these therapies is inconclusive.[15] The review limited its focus on those therapies often administered by nurses (TT, HT, and Reiki). Overall, the number of studies specifically addressing cancer pain was small (n = 4). All but one study contained significant methodological flaws, and although the existing studies suggest efficacy, the authors expressed concern that publication bias is likely given that negative study results often remain unpublished. A 2011 systematic review of energy healing for cancer included eight studies (six quantitative and two qualitative). Quality was assessed using the Scottish Intercollegiate Guidelines Network (SIGN) quality scale. Authors determined that none of these studies were of sufficient size or quality to allow conclusions about efficacy.[16] A later 2014 qualitative literature review of biofield therapies for cancer symptoms, again for oncology nurses and limited to TT, HT, and Reiki, included 13 studies assessing the main cancer-related outcomes of pain, anxiety, fatigue, and quality of life, and included several of the same studies covered in the aforementioned reviews. These authors found again that most studies were descriptive or of quasi-experimental design, were inadequately powered, and contained diverse methodological flaws.[15]

A 2010 RCT of medical qi gong for cancer patients (n = 162) assessed the effects on quality of life, fatigue, and mood using validated instruments and included changes in biomarker (CRP) for inflammation.[18] This study was adequately powered. However, volunteers were recruited for the study, had a variety of cancer types, and none of the participants or the qi gong instructors were blinded to the condition, introducing some selection and experimental bias. There was no active control group to help control for non-specific effects of the qi gong intervention. In addition, there was a relatively low completion rate (76%). Compared to the control group, the medical qi gong group experienced significant improvement in overall quality of life (mean difference between groups 9.0; 95% CI, 5.62-12.36; $P < 0.001$), fatigue (mean difference between groups 5.70; 95% CI, 3.32-8.09; $P < 0.001$), mood disturbance (mean difference between groups -10.64; 95% CI, -19.81 to -1.47; $P < 0.021$), and inflammation/CRP level (mean difference between groups -23.17; 95% CI, -37.08 to -9.26; $P < 0.044$).

A 2011 NIH NCCAM randomized, three-armed control study of polarity therapy for cancer-related fatigue showed significant effect size for improving daily fatigue for patients receiving polarity therapy compared to standard care or an active control group receiving modified massage therapy ($P = 0.05$). The study population consisted of 45 women with breast cancer who were receiving radiation therapy for non-metastatic breast cancer; it was considered a pilot study for assessing effect sizes. Quality-of-life outcomes were also measured and decreased in all groups, but least of all in the polarity therapy group, suggesting a beneficial effect on quality of life using polarity therapy for cancer patients undergoing treatment.[19]

Anderson and Taylor also provided a descriptive review of biofield research for cardiovascular symptoms. This review concluded that studies contained methodological flaws, making conclusions about efficacy of therapies difficult, but the individual descriptions of these studies did not assess study designs or methodologies in detail, placing more emphasis on describing chosen measures and results, which were largely reported as beneficial.[20]

Friedman et al reported in a correspondence that the effects of Reiki treatment on heart rate variability (HRV) in a randomized, controlled, three-armed trial.[21] Low HRV is associated with increasing age and risk of sudden cardiac death, and higher HRV reflects increased parasympathetic tone, which has been shown to be protective in acute coronary syndrome. Forty-nine patients recovering from acute coronary syndrome and meeting inclusion criteria were divided into one of three groups: a treatment group receiving intervals of Reiki therapy, a control group instructed to rest quietly during treatment intervals, and an active control group that listened to music during the treatment intervals. Changes in high-frequency HRV were measured from continuous ECG monitoring during treatment intervals. Secondary outcomes included screening for changes in negative and positive emotions. Reiki exerted a significant effect on

increasing high-frequency HRV compared to rest (P = 0.025) and music control (P = 0.007) groups. Significant increases in positive emotions and decreases in negative emotions were noted on a seven-point Likert scale for the patients treated with Reiki compared to control groups.

A 2009 systematic review of Reiki research reported 12 trials that met inclusion criteria: a human study published in English, a control arm, and an intervention provided by a Reiki practitioner.[22] Authors applied modified CONSORT (Consolidated Standards of Reporting Trials) criteria to the studies, and all had deficits in at least one of three key areas: randomization, blinding, and accountability of all patients. Jadad quality scores (a process for assessing clinical trial quality methodology) were determined for each trial. Although nine of the 12 trials studied showed therapeutic effect, 11 out of 12 were ranked "poor" by Jadad scores. Thirty-one outcomes for these 12 clinical trials were reported, suggesting that researchers are still attempting to understand the breadth of potential Reiki benefits. Despite individual studies showing statistically significant benefits for the outcomes studied (in some cases $P \leq$ 0.0001), the overall quality standards of the studies were poor, creating concern about bias, validity, and causal inference.

TT was a focus of two recently published Cochrane review updates: for anxiety disorders (2009) and wound healing (2012). Only 11 studies on TT for anxiety disorders were uncovered in the literature search, and none of these studies met inclusion criteria.[23] The TT for wound healing review resulted in four studies adequately meeting inclusion criteria. All trials were in people with experimental wounds. Two trials of relatively small numbers (n = 44 and n = 24) showed significant increase in healing of wounds with TT: one trial showed no significant treatment affect, and the other showed worse healing after TT. Pooling the studies for analysis showed no significant difference in complete wound healing (relative risk, 1.03; 95% CI, 0.12-8.60). The authors assessed all the included trials as having high risk of bias and being of poor study quality in general.[24]

Thought field therapy (TFT) efficacy for anxiety was studied in a 2012 RCT. Although results suggested that TFT had an enduring effect on reducing anxiety, the study included only a waitlist control group, which failed to control for the non-specific effects of the intervention. Further, the patients included in the study were not restricted in their use of medication and other therapies during the study period, introducing potential confounding variables.[25]

Roe's meta-analysis, reported above, also included a second analysis of 57 human studies meeting inclusion criteria. A small but significant effect size r of 0.115 was determined in this analysis, still indicating better outcomes for the energetic interventions compared to no treatment or placebo, although the authors cited generally poor methodology and evidence of publication bias limiting unequivocal conclusions.[10]

CONCLUSION

To date, there is statistically significant evidence that energy medicine may be helpful for low-grade reduction of pain intensity. There remains insufficient high-quality research to support decisions to use energy therapies as treatment or adjunctive therapy for other medical conditions, or even other dimensions of the pain experience. There are, thus far, no reported risks for these therapies, and many are offered by volunteers or as part of normal nursing care and are "free." As Ferraresi et al stated in a review of these therapies, for use in the dialysis ward, controversial efficacy needs to be balanced against no side effects, frequent availability at no cost (hospital nursing practice and volunteers), and easy, risk-free integration with other conventional and pharmacologic therapies.[26] Thus, energy therapies support ethical principles of beneficence (they are possibly beneficial), non-maleficence (they are non-harmful), justice (they are accessible), and autonomy (they are often preferred and chosen by patients), and for these reasons alone can be recommended as adjunctive therapeutic interventions for patients who are open to using them while we await the necessary high-quality research on their efficacy. ■

REFERENCES

1. Sharaf MR. *Fury on Earth: A Biography of Wilhelm Reich*. New York: St Martin's Press; 1983.
2. Barnes PM, et al. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data* 2004;343:1-19.
3. Radin DI. Event-related electroencephalographic correlations between isolated human subjects. *J Altern Complement Med* 2004;10:312-323.
4. Standish LJ, et al. Electroencephalographic evidence of correlated event-related signals between the brains of spatially and sensory isolated human subjects. *Altern Ther Health Med* 2004;10:307-314.
5. Standish LJ, et al. Evidence of correlated functional magnetic resonance imaging signals between distant human brains. *Altern Ther Health Med* 2003;9:121-125.
6. Achterberg J, et al. Evidence for correlations between distant intentionality and brain function in recipients: A functional magnetic resonance imaging analysis. *J Altern Complement Med* 2005;11:965-971.
7. Uchida S, et al. Effect of biofield therapy in the human brain. *J Altern Complement Med* 2012;18:875-879.
8. Pike C, et al. Asymmetric activation of the anterior cerebral cortex in recipients of IRECA: Preliminary evidence for energetic effects of an intention-based biofield treatment modality on human neurophysiology. *J Altern Complement Med* 2014;10:780-786.
9. Abe K, et al. Effect of a Japanese energy healing method known as Johrei on viability and proliferation of cultured cancer cells in vitro. *J Altern Complement Med* 2012;18:221-228.
10. Roe C, et al. Two meta-analyses of non-contact healing studies. *Explore* 2015;11:11-23.
11. Rindfleisch A. Human Energetic Therapies. In: Rakel D, ed. *Integrative Medicine* 3rd ed. Philadelphia: Elsevier Saunders; 2012:980-987.
12. Jain S, et al. Biofield therapies: Helpful or full of hype? A best evidence synthesis. *Int J Behav Med* 2010;17:1-16.
13. Anderson J, Taylor AG. Effects of healing touch in clinical practice. *J Holist Nurs* 2011;29:221-228.
14. So PS, et al. Touch therapies for pain relief in adults (review). *Cochrane*

Database Syst Rev 2008; Issue 4. Art. No.: CD006535. DOI: 10.1002/14651858.CD006535.pub2.
15. Anderson J, et al. Biofield therapies and cancer pain. *Clin J Oncol Nurs* 2012;16:43-48.
16. Agdal R, et al. Energy healing for cancer: A critical review. *Forsch Komplementmed* 2011;18:146-154.
17. Gonella S, et al. Biofield therapies and cancer-related symptoms: A review. *Clin J Oncol Nurs* 2014;18:568-576.
18. Oh B, et al. Impact of medical Qigong on quality of life, fatigue, mood and inflammation in cancer patients: A randomized controlled trial. *Ann Oncol* 2010;21:608-614.
19. Mustian KM, et al. Polarity therapy for cancer-related fatigue in patients with breast cancer receiving radiation therapy: A randomized controlled pilot study. *Integr Cancer Ther* 2011;10:27-37.
20. Anderson JG, et al. Biofield therapies in cardiovascular disease management: A brief review. *Holist Nurs Pract* 2011;25:199-204.
21. Friedman RS, et al. Effects of Reiki on autonomic activity early after acute coronary syndrome. *J Am Col Cardiol* 2010;56:995-996.
22. VanderVaart S, et al. A systematic review of the therapeutic effects of Reiki. *J Altern Complement Med* 2009;15:1157-1169.
23. Robinson J, et al. Therapeutic touch for anxiety disorders (review). *Cochrane Database Syst Rev* 2007; Issue 3. Art. No.: CD006240. DOI: 10.1002/14651858.CD006240.pub2.
24. O'Mathuna DP, et al. Therapeutic touch for healing acute wounds (review). *Cochrane Database Syst Rev* 2012, Issue 6. Art. No.: CD002766. DOI: 10.1002/14651858.CD002766.pub2.
25. Irgens A. et al. Thought Field Therapy (TFT) as a treatment for anxiety symptoms. *Explore* 2012;8:331-338.
26. Ferraresi M, et al. Reiki and related therapies in the dialysis ward: An evidence-based and ethical discussion to debate if these complementary and alternative medicines are welcomed or banned. *BMC Nephrol* 2013;14:129.

CARDIOVASCULAR DISEASE

ABSTRACT & COMMENTARY

Do Multivitamin-mineral Supplements Protect Against CVD Mortality?

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SYNOPSIS: An association was found between decreased death from cardiovascular disease and U.S. women's use of multivitamin-mineral supplements when taken for at least 3 years. A similar association was not found for men, nor for either gender after use of multivitamins without minerals.

SOURCE: Bailey RL, et al. Multivitamin-mineral use is associated with reduced risk of cardiovascular disease mortality among women in the United States. *J Nutr* 7 Jan 2015; ePub ahead of print. doi: 10.3945/jn.114.204743.

The overall general finding from this analysis of a representative sample of U.S. adults was that no significant associations were found between the use of multivitamin-mineral supplements (MVMs) or multivitamins (MVs) and cardiovascular disease (CVD) mortality when all supplement users were compared with nonusers. However, when users were grouped according to how long they had been using supplements, some significant associations were found. Those who used MVMs for more than 3 years had a significant reduction in hazard ratio (HR) compared to non-users (HR, 0.65; 95% confidence interval [CI], 0.49-0.85). When further subdivided by gender, the association between women using MVMs for more than 3 years and non-users was strengthened (HR, 0.56; 95% CI, 0.37-0.85). No significant association was found for men (HR, 0.79; 95% CI, 0.44-1.42). Significant associations were not found for MVs and CVD mortality.

In this study, data from the National Health and Nutrition Examination Survey III (NHANES III) were matched with mortality data from the National Health Index (NHI) through the end of 2011 to examine potential associations between MVM or MV use and CVD mortality. NHANES III allows the selection of a nationally representative sample of the U.S. population. Participants were enrolled between 1988 and 1994 and were interviewed at baseline about their supplement use. During the initial interview, participants showed researchers the containers and labels of all supplements they were taking. This allowed the collection of more detailed information on supplement contents and doses than is often available in studies. Based on length of use reported, participants were assigned to one of three groups: those using supplements for < 1 year, for 1-3 years, or ≥ 3 years. For this study, an MVM was defined as a product containing three or more vitamins plus one or more minerals. An MV was defined as any vitamin combination that did not include minerals.

The current analysis was based on adults older than 40 years of age in 2011 who had no history of CVD, myocardial infarction, stroke, coronary heart disease, or chronic kidney disease at baseline. Pregnant and lactating

Summary Points

- The mortality from cardiovascular disease (CVD) was significantly associated with taking multivitamin-mineral (MVM) supplements for 3 years or longer for healthy U.S. women.
- A similar statistically significant association was not found for men.
- No significant associations were found for use of multivitamins without minerals and CVD mortality.
- Several statistical tests were performed to check the results' reliability, and these confirmed the study's conclusions. However, the findings need to be interpreted with caution because of the nature of the study design involved.

women and anyone with missing dietary supplement data were excluded. The final study sample was 8678 participants. The median length of time between NHANES III baseline and NHI report was 18.7 years. Among the population analyzed, 45.3% had used any form of dietary supplement in the previous 30 days. The most frequently used type of supplement was an MVM (21.2%), followed by an MV (14.2%). Up to the end of 2011, 4122 NHANES III participants had died, with CVD being the most common cause of death (1636 participants or 40% of deaths).

■ COMMENTARY

MVs are the most frequently used dietary supplement in the United States, with Americans spending an estimated $11.8 billion on them each year.[1] The Bailey et al study provides important evidence about the effectiveness of MVM supplements for the prevention of death from CVD. At the same time, its findings raise additional questions about MVMs and CVD and how best to study their effectiveness. The U.S. Preventive Services Task Force concluded in 2013 that there was no evidence of an effect of nutritional doses of vitamins or minerals on CVD, cancer, or mortality in healthy individuals.[1] However, this systematic review identified only two randomized, controlled trials (RCTs) upon which to base its recommendations. One of these RCTs enrolled only male U.S. physicians and found no association between MVM use and CVD incidence or mortality after 11 years. The other RCT enrolled men and women, and found no statistically significant effect on CVD incidence after 7.5 years, but used a supplement containing antioxidants and was not an MVM. On the other hand, a prospective cohort study in Sweden found that MV use by women for more than 5 years was associated with a reduced risk of myocardial infarction.[2] An RCT of MVM use by women and CVD mortality is not available.

Untangling the results of research on MVs from MVM products is difficult. Part of the problem behind the inconsistent findings has to do with the study designs. The RCT is regarded as the gold standard for determining whether an intervention is effective. But as the study becomes more controlled, the setting becomes less like everyday life and the subjects become less heterogeneous. RCTs are more narrowly focused, which can make it more difficult to apply their findings to the general population. On the other hand, observational studies like this one include a more representative spread of people from all walks of life. They allow people to continue living their usual lifestyle, but then it becomes more difficult to separate the impact of the intervention from the many confounding factors. To take account of this, Bailey et al ran several statistical tests and found similar findings each time.

The researchers did highlight some additional important limitations with their study. The participants' use of supplements was self-reported and only collected at baseline in NHANES III. Over the course of the next 18 or so years, participants could have changed their use of supplements in any number of ways. This is a major limitation with the findings, especially since the intervening years are the most important for any assessment of the impact of the supplements on CVD. In addition, NHANES III was conducted before the passage of the Dietary Supplement and Health Education Act of 1994. Since then, dietary supplement use has increased in general in the United States.[3] In addition, those who had been taking supplements for 3 years prior to NHANES III may have been "early adopters" who were proactive about their health in other ways.

Another reason for variation in the findings of different studies arises from the different supplements used for different lengths of time. Although NHANES III identified the products each participant used, they varied widely. In addition, other studies have administered individual vitamins and minerals in varying doses, or MVs. Although MVMs are the most widely used supplements in the United States, few RCTs have used MVM supplements. Results will inevitably remain variable given that the interventions are variable. Why MVMs have benefits not found with MVs is unclear. Minerals (like magnesium or copper) may have their own beneficial effects on CVD, although many of these individual effects are themselves uncertain. The reasons for gender differences are also unclear. The limitations of observational studies must be kept in mind, and also the challenges of sub-group analyses.[4] As more sub-groups are analyzed within study results, the more likely it is to find spurious correlations and significant findings. Sub-group analyses are best used to generate hypotheses that are tested in RCTs.

Overall, Bailey et al found some evidence that MVMs may have a protective effect against CVD mortality in healthy U.S. women when used for at least 3 years. At the same time, the study provides little evidence of benefit for men against CVD mortality, and no evidence of benefit from MV products. While this study was well-designed, it has important limitations given the data available for analysis. Healthy women can be encouraged that MVMs may protect against CVD mortality, although a clearer recommendation will have to await the results of further studies, especially the results of RCTs of specific MVM supplements. ■

REFERENCES

1. Fortmann SP, et al. Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: An updated systematic evidence review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2013;159:824-834.
2. Rautiainen S, et al. Multivitamin use and the risk of myocardial infarction: A population-based cohort of Swedish women. *Am J Clin Nutr* 2010;92:1251-1256.
3. Gahche J, et al. Dietary supplement use among U.S. adults has increased since NHANES III (1988–1994). *NCHS Data Brief* 2011;61:1-8.
4. Horton R. From star signs to trial guidelines. *Lancet* 2000;355:1033-1034.

DIGESTIVE DISORDERS

ABSTRACT & COMMENTARY

Gut Check — Mindfulness in the Setting of Ulcerative Colitis

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Dr. Greenfield reports no financial relationships relevant to this field of study.

SYNOPSIS: Disappointing results from this double-blind, time-/attention-controlled study would cast doubt on the potential benefits of mindfulness-based stress reduction for people with moderately severe ulcerative colitis were it not for the presence of significant shortcomings in study methodology.

SOURCE: Jedel S, et al. A randomized controlled trial of mindfulness-based stress reduction to prevent flare-up in patients with inactive ulcerative colitis. *Digestion* 2014;89:142-155.

Ulcerative colitis (UC) is a chronic inflammatory disorder primarily affecting the mucosal lining of the colon and rectum. The disease course of UC is marked by variable periods of remission and flare-up with symptoms including abdominal pain, diarrhea, and rectal bleeding. An underlying cause for the disease has yet to be determined, and there is presently no cure. As such, clinical management is focused on reducing frequency and severity of flare-ups and associated complications, with heavy reliance on prescription medication such as prednisone, immunosuppressants, and biologics.

However, research strongly suggests that psychosocial stress can initiate the body's pro-inflammatory cascade and potentially induce UC flare-ups. By extension, there has been growing interest in the use of stress-reduction techniques to help modulate disease activity in disorders having an inflammatory component. One of the most promising approaches is mindfulness-based stress reduction (MBSR), originally championed by Jon Kabat-Zinn and now offered in clinics around the globe.[1] Mindfulness defines a state of focused attention that can be described as awareness of experience without evaluation or judgment.[2] Data suggest that MBSR may offer therapeutic benefit in a variety of clinical settings, including mood disorders, chronic pain, cancer, post-traumatic stress disorder, and conditions characterized by inflammation. The aim of this randomized (concealed),

Summary Points

- Ulcerative colitis (UC) is a chronic inflammatory disorder primarily affecting the mucosal lining of the colon and rectum. Clinical experience suggests that psychosocial stress may induce disease flare-ups.
- Mindfulness-based stress reduction (MBSR) is an effective stress management technique that often enhances a person's ability to cope with difficulties.
- This small, randomized, controlled trial largely failed to show meaningful clinical improvement in subjects with moderately severe UC in remission who practiced MBSR as opposed to controls. Methodological shortcomings were significant.

double-blind, time-/attention-controlled study was to investigate the effects of MBSR on disease course (flare frequency), quality of life (QOL), markers of inflammation, and psychological parameters in people with moderately severe UC in remission over a 12-month period.

Patients aged 18-70 years were recruited from the Rush University Medical Center Inflammatory Bowel Disease (IBD) Clinic and the Greater Chicago area. Inclusion criteria included moderately severe but inactive UC (confirmed in all subjects through physical examination and sigmoidoscopy), at least one flare-up within the past 6 months, and taking no IBD medication or on a stable dose for at least 3 weeks prior to enrollment. Exclusion criteria included use of antibiotics within the prior month or anti-diarrheal medications within the previous week, unresolved history of physical or sexual abuse, current or past dissociative disorder, history of psychosis or prior hospitalization for self-harm/suicidal ideation, and prior mind/body therapy training. A clinical psychologist screened prospective subjects for psychiatric eligibility.

Participants were advised that they would be randomized to one of two courses of mind/body therapy, neither of which had been rigorously tested in people with UC but that were associated with health benefits in other settings. Baseline data (including self-report questionnaires, serum samples, 24-hour urine and stool collection) were collected at the first study visit, and subjects were assigned to either MBSR or a time-/attention-control group. The MBSR program followed the 8-week curriculum developed by Kabat-Zinn,[3] including weekly 2.0-2.5 hour sessions of instruction in formal exercises such as sitting meditation, body scans, and yoga postures as well as more informal practices aimed at promoting mindfulness in everyday life. Homework assignments involved 45 min/day of CD-guided MBSR 6 days per week. A physician or psychologist with significant personal MBSR experience taught the courses. The control group was assigned eight sessions of slightly shorter duration in which information on stress and its physical effects was shared via lecture or video (program intended to control for time, support, and attention). Subjects started their programs within 1 month of baseline assessment. For both courses, compliance was defined as attendance at a minimum of five classes.

Assessments occurred at baseline (visit 1, pretreatment visit), post 8-week course (visit 2, weeks 9-12), and at 6- and 12-month follow-ups (visits 3 and 4). Data analysis was initiated only after all subjects had completed the study. If a UC flare-up developed at any point, the subjects completed their assessments and were then removed from the study. Primary outcome of interest was disease status defined as Mayo UC-DAI > 2 (a commonly employed composite measure of UC disease activity that accounts for stool consistency, rectal bleeding, findings on endoscopy, and physician global assessment), plus a rectal bleeding score > 2 and sigmoidoscopy score of > 2. Secondary outcomes of interest included changes in markers of inflammation and disease activity (calprotectin levels, cytokines [IL-6, IL-8, IL-10], CRP, the Inflammatory Bowel Disease Quality-of-Life (QOL) Questionnaire [IBD-Q]), as well as markers of stress and psychological assessments (serum ACTH, the Perceived Stress Questionnaire [PSQ], the Beck Depression Inventory [BDI], the State-Trait Anxiety Inventory (STAI), the Mindful Attention Awareness Scale [MAAS], and the Perceived Health Competence Scale [PHCS]). Intention-to-treat analysis was performed; participants who flared during the intervention were included in the analysis.

A total of 55 subjects met inclusion criteria and underwent randomization. Subjects in the MBSR group were about 7 years older than those in the control group at the time of UC diagnosis, had less severe symptoms, and were significantly older at time of participation in the study. Patients in both groups had moderately severe UC, with more than 40% being prednisone-dependent and averaging two flare-ups during the year prior to enrolling in the study. Two participants (one in each group) dropped out during their 8-week courses, while two patients randomized to MBSR and one in the control group attended fewer than five classes.

At the end of the study, no statistically significant difference existed between the two groups with respect to disease activity, the primary outcome of interest (number of flare-ups 13/27 = 48% MBSR group, 14/26 = 54% controls). Regarding secondary measures, no differences between the two groups were detected for calprotectin levels associated with flare-ups, or for time to and severity of flare-up. Serum levels of the anti-inflammatory cytokine IL-10 increased in patients in the MBSR group who flared, whereas IL-10 levels decreased in control group members who experienced a flare-up. Mixed-model analysis revealed significantly better QOL among subjects with UC flare-ups in the MBSR group compared to flared control group members as measured by the IBD-Q Total Scale ($P = 0.001$) and the bowel ($P = 0.01$) and emotion ($P = 0.01$) subscales, respectively. Among patients who experienced flare-ups, those in the MBSR group demonstrated significantly lower PSQ total (55.17 ± 8.66) and index scores (0.29 ± 0.10) at last visit. There were, however, no differences between members of the two groups, with flare-ups on measures of depression, anxiety, mindfulness, or perceived health competence (BDI: $P = 0.64$; STAI: $P = 0.12$; MAAS: $P = 0.91$; PHCS: $P = 0.30$). Likewise, there were no differences between MBSR and control groups on measures of depression (BDI: $P = 0.75$), anxiety (STAI: $P = 0.92$), mindfulness (MAAS: $P = 0.43$), or perceived health competence (PHCS: $P = 0.33$) at last visit among participants who did not experience a flare.

Post-hoc analysis showed that MBSR group subjects with the most severe symptoms at baseline (upper tertile of the IBD-Q Bowel Subscale) demonstrated a positive effect of MBSR as compared to those exhibiting less severe symptoms (upper tertile vs lower tertile, $P < 0.001$), something not observed in the control group. In addition, MBSR subjects within the highest tertile of baseline PSQ scores experienced a reduced flare-up rate compared to controls in the highest tertile. Flare rate among MBSR group subjects in the top tertile of baseline cortisol levels was reduced compared to controls with comparable baseline cortisol.

The authors conclude that MBSR did not affect the rate or severity of flare-ups in UC patients with moderately severe disease in remission, but that MBSR might be effective for those with high levels of perceived stress and urinary cortisol measures during remission. MBSR might improve QOL in similar UC patients who experience disease flare-ups by encouraging non-judgmental acceptance of their circumstances, thereby reducing any negative impact on QOL.

■ COMMENTARY

It is, of course, far easier to sit in judgment of published research than to identify a problem that needs a solution, develop a research protocol, perform the study, assess the results, and finally share one's findings in peer-reviewed literature. The research team behind the present work authentically deserve praise for their efforts, yet bear responsibility for significant methodological flaws (which they accept in the paper) that would have relegated any findings to a footnote worthy of interest at best and, at worst, to an opportunity lost. Unfortunately, the paper in question reads more like the latter.

The seed of the study makes good sense — MBSR has shown promise in numerous clinical scenarios. Since UC flare-ups and psychosocial stress seem intimately related, one could reasonably assume that MBSR would offer potential benefit in the setting of moderately severe disease. Positive findings from the trial are few and far between, although the importance of a positive effect on QOL measures should not be minimized. The results do not, however, suggest a meaningful clinical impact of MBSR on disease course or measures of inflammation in subjects with moderately severe UC. On the surface, this may be surprising, but the results were doomed from the outset due to factors including small sample size, significant baseline differences between the two groups, and a control group well-matched for time but not for attention and support. In addition, while the MBSR course was taught by practitioners with lengthy personal experience, it is unknown if the instructors were actually certified as MBSR trainers. A person long-committed to a practice is not necessarily an effective instructor in that practice, and individual response to training often varies based on the trainer's skill, and, perhaps, their interpersonal skills.

In the end, and in the face of disappointing results, the research team offered that MBSR is a low-risk intervention that may still be of benefit to select patients with UC who respond poorly to psychosocial stress, even if it does not significantly impact disease course. That conclusion existed in the minds of many practitioners before the study began, and is neither burnished nor dulled by its publication due to the aforementioned shortcomings. Many prior studies suggest that MBSR can be a valuable tool in helping people cope with life's challenges and uncertainties, even in the absence of an impact on clinical symptoms. A future paper by the researchers will address relevant findings of the interventions on stool microbiota, but their methodology will remain a weakness. MBSR is a promising intervention in various clinical settings, including UC. The research efforts behind this paper, though laudable, have unfortunately not borne clinically useful fruit. ■

REFERENCES

1. Kabat-Zinn J. Mindfulness-based interventions in context: Past, present, and future. *Clin Psychol Sci Pract* 2003;10:144-156.
2. Selfridge N. Mindfulness based stress reduction: Non-doing for well-being. *Altern Med Alert* 2011;14:56-60.
3. Kabat-Zinn J. *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress*, Pain and Illness. New York, Delacorte Press; 1990.

WOMEN'S HEALTH

ABSTRACT & COMMENTARY

Topical Curcumin for Treatment of Lactational Mastitis

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Dr. Haas reports no financial relationships relative to this field of study.

SYNOPSIS: In comparison to placebo, topical curcumin improves markers of lactational mastitis within 72 hours of administration.

SOURCE: Afshariani R, et al. Effectiveness of topical curcumin for treatment of mastitis in breastfeeding women: A randomized, double-blind, placebo-controlled clinical trial. *Oman Med J* 2014;29:330-334.

Through a randomized, double-blind, placebo-controlled clinical trial, the authors set-out to assess the anti-inflammatory effects of topical curcumin in patients with lactational mastitis. The authors identified topical curcumin as a possible treatment for this diagnosis given its ease of use early in the development of symptoms, in addition to its perceived benign side effect profile, especially compared to non-steroidal anti-inflammatory drugs.

Given the wide spectrum of symptoms among women suffering from lactational mastitis, an inflammation severity index was used to screen patients for inclusion. An initial criterion for mastitis was defined as meeting any two of the following: breast erythema, increased breast tension not relieved by breastfeeding, pain in the breast, flu-like symptoms (including fever > 39° C) and lumps in the breast tissues. Only those patients with moderate mastitis were included in the study, as determined by a scoring system grading the severity of erythema, breast tension, and breast pain. Exclusion criteria included: milk staphylococcal count higher than 10^4 CFU/mL, milk leukocyte count higher than 10^6 CFU/mL, breast abscess, breast engorgement, breast filling defect, blocked duct, galactocele, previous history of mastitis or recurrent mastitis, recent trauma to the affected breast, previous breast surgery, inflammatory skin diseases, and/or mothers exposed to systemic antibiotics within the last 2 months.

Patients were randomized to treatment consisting of either topical curcumin cream (standardized to 200 mg curcumin per pump) or topical moisturizer cream to be applied every 8 hours for 72 hours. Prior to randomization, all subjects were taught effective techniques for breast milk removal. Symptom severity, as discussed above, was assessed by the same staff nurse every 24 hours during the 72-hour treatment period.

Based on their power analysis, the authors enrolled 70 participants, 64 of whom were randomly assigned to either the treatment or placebo group (four did not meet inclusion criteria and two declined participation). Blinding reportedly failed for one participant, resulting in 32 patients in the curcumin group and 31 patients in the placebo group. No significant differences were reported between the two study groups regarding baseline characteristics; however, only age and duration of lactation (months) were discussed with no supporting table illustrating other demographic characteristics. No dropouts were reported.

After the 72-hour intervention period, 72% of patients in the curcumin group experienced complete resolution of the predetermined signs/symptoms of mastitis compared to 39% of patients in the placebo group ($P < 0.001$). Moreover, although both groups experienced significant reductions in pain scores, the curcumin group reported significantly lower scores for pain compared to the placebo group, 0.47 vs 3.13, respectively ($P < 0.001$). The authors also reported that curcumin application improved scores of breast tension and pain within the first 48 hours of treatment, while significant improvements in erythema typically occurred during the last 24 hours of treatment. No adverse events were reported for either the treatment or placebo group.

Summary Points

- Topical curcumin can successfully treat moderate lactation mastitis within a 72-hour period.
- Breast pain and tension are the first symptoms to improve with topical curcumin application, with erythema resolving later.
- The formulation used was a cream delivering 200 mg of curcumin per pump.

■ COMMENTARY

Curcumin, one of a family of compounds isolated from turmeric rhizome (*Curcuma longa*), has garnered a growing interest in the treatment of a variety of inflammatory conditions, including dermatological conditions such as scleroderma and psoriasis.[1] The authors of this study insightfully sought to determine the efficacy of topical curcumin in the treatment of an important inflammatory skin disorder among breastfeeding mothers, lactational mastitis. Through the use of a randomized, double-blind, placebo-controlled study, the authors provide compelling evidence about the utility of topical curcumin for treating moderate mastitis. Interestingly, the authors limited their study to moderate mastitis and excluded those patients with mild classification. Agreeably, it was prudent to exclude those with severe mastitis in lieu of conventional treatment. However, including those with mild mastitis might have enhanced the generalizability of the study, especially as participants were recruited after referral to a specialty maternal/child health care center, presumably from another physician such as a primary care provider. Perhaps treatment of mild mastitis with topical curcumin could have prevented progression to more advanced stages of mastitis? Nonetheless, the present study supports the use of topical curcumin for wound healing and illustrates some of its known healing properties, such as the induction of a large infiltration of immunological

cells (macrophages, neutrophils and fibroblasts), and the production of a strong anti-inflammatory effect.[2]

A few other points should be considered before recommending topical curcumin to breastfeeding mothers. Limited baseline demographic information was provided, as mentioned above. The number of prior pregnancies or prior breastfeeding experiences would have been helpful to assess differences between the two groups. A mother with prior breastfeeding experience would likely be able to circumvent the development or progression of mastitis, which would have been an important variable for consideration. On another note, during treatment, blinding reportedly failed for one participant without further mention of the circumstances surrounding the incident. Further information would have been helpful to dispel any questions regarding the reliability of blinding among other subjects. Along a similar vein, some discussion regarding funding or acquisition of topical preparations would have been important to note. The company providing the topical curcumin preparation offers the product online for approximately $30 per bottle, arguably above many mothers' prescription copays. Finally, despite the relative safety of high-dose curcumin therapy,[3] the study did not evaluate the side effects of the topical treatment. Presumably the side effects of topical application to breastfeeding mothers would have been minimal; however, considerations should be given to the infants ingesting the curcumin, although application of the topical curcumin direct after feeding times would eliminate this concern. ■

REFERENCES

1. Thangapazham RL, et al. Beneficial role of curcumin in skin diseases. *Adv Exp Med Biol* 2007;595:343-357.
2. Jacob A, et al. Mechanism of the anti-inflammatory effect of curcumin: PPAR-gamma activation. *PPAR Res* 2007;2007:89369.
3. Nguyen TA, Friedman AJ. Curcumin: A novel treatment for skin-related disorders. *J Drugs Dermatol* 2013;12:1131-1137.

CME QUESTIONS

1. **Which of the following biological measures has NOT been reported to be influenced by energy therapies or distant intention?**
   a. MRI
   b. fMRI
   c. ECG
   d. CRP

2. **Which of the following statements is true?**
   a. Ulcerative colitis is typified by so-called "skip lesions" and affects the entire bowel wall.
   b. MBSR represents a typical form of clinical hypnosis.
   c. Stress reduction techniques have never been found to affect physical manifestations of disease.
   d. MBSR may benefit select patients with ulcerative colitis who lack effective coping skills and respond poorly to psychosocial stress.

3. **The findings from the study of multivitamin-mineral supplements suggest that healthy U.S. women benefit from taking:**
   a. multivitamin supplements for at least 3 years to protect against cardiovascular disease mortality.
   b. multivitamin-mineral supplements for 2 years to protect against cardiovascular disease mortality.
   c. multivitamin-mineral supplements for at least 3 years to protect against cardiovascular disease mortality.
   d. multivitamin-mineral supplements for at least 3 years to protect against cancer.

4. **The use of a topical curcumin preparation resolves moderate lactational mastitis in approximately what percent of cases in the present study?**
   a. < 25%
   b. 25-50%
   c. 50-75%
   d. > 75%

[IN FUTURE ISSUES]

Aromatherapy

Biofeedback for headache

Blueberries and CVD in postmenopausal women

Acupuncture for irritable bowel syndrome