

Clinical Research into Alternative and Complementary Therapies: How Do We Tell If the Glass Is Half Empty or Half Full?



This issue of *The Journal* contains a report by Astin, *et al* that compares the efficacy of mindfulness meditation and Qigong movement therapy to education, in individuals with fibromyalgia (FM)¹. The study is commendable, and superior to most studies of complementary and alternative therapies, in many respects, because (1) the sample size was adequate (total randomized 128); (2) participants were randomized to receive either the active treatment or a “control” condition: in this case an education group that received the same number of hours of “contact” time; and (3) suitable outcome measures and analysis strategies were used. The principal results of the study were that, although patients with FM receiving mindfulness meditation and Qigong movement noted significant improvements in most outcomes, similar improvements were noted in the group receiving only education. The improvements in both groups were clinically significant and sustained (to 24 weeks).

A quick read of this study may lead to an inappropriate conclusion: that this is a negative study that tells us nothing about what we may be able to do to help our patients with FM. But it is worthwhile to at least consider that “the glass is half full,” and that this particular study gives us some guidance into what treatments might help patients with FM. More important, it is useful to reflect on how the design of this and other such studies may influence their interpretation.

The first conundrum with interpreting the results of this and similar studies is that the control group is not receiving an “inert” treatment. The control group received the same number of hours of contact (20) as the active treatment group. During this contact, the participants randomized to the control group received education regarding a variety of aspects of self-management, modeled after the Arthritis Foundation self-help courses². This program contained elements of both exercise and cognitive behavioral interventions, both of which have been shown to be moderately effective therapies, not only in FM but for most other chronic medical conditions³⁻⁵.

Thus, in designing an “efficacy” study that conformed to

the highest scientific principles, the authors “set the bar” very high; the active intervention would have had to be extremely efficacious to show superiority over a treatment known to be effective. Rheumatologists that may be more familiar with interpreting the results of pharmacological rather than behavioral interventions could consider this an “active comparator” rather than “placebo-controlled” study, analogous to a study comparing a new analgesic to an approved nonsteroidal antiinflammatory drug, rather than to an inert placebo.

This raises a fundamental problem with performing research into non-drug interventions, including most complementary and alternative therapies. For the results to be believable and credible, we usually turn to efficacy designs, and compare these treatments to “sham” or “contact control” that may not be entirely inert. It is difficult for any new treatment to show superiority over an existing treatment that is already known to be effective.

To avoid this bias against showing an effect of their active intervention, the authors could have used one of several alternative designs. One option would have been to purposely “dilute” the effectiveness of the control intervention, by having the therapist spend 20 hours with participants, but not give instructions that might lead to improvements in symptoms. But this too would likely bias the study results, in this case by leading to a selectively higher dropout rate in the control arm of the study.

Another option for the authors would have been to concede that it is difficult to perform an “efficacy” study of this type of intervention, and instead perform an “effectiveness” study. Such designs have been common in behavioral interventions for some time, and typically do not attempt to control for issues such as contact time. Instead, effectiveness studies examine how well an intervention works in a “real-life” setting, usually examining the incremental effect of an intervention as compared to a group randomized to receive “usual and customary care.” Such designs do help control for some potential problems with interpreting the

See The efficacy of mindfulness meditation plus Qigong movement therapy in the treatment of fibromyalgia, page 2257

results of “open” studies, such as the tendency to spontaneous improvement because of the natural history of the disorder, or “regression to the mean” (because individuals tend to enroll in clinical trials when their symptoms are worse). Unfortunately, the natural history is that patients with FM do not spontaneously improve, and do not necessarily improve even with treatment⁶. Thus, both the magnitude of improvement seen in this study and the fact that this lasted for 24 weeks are unlikely to have been due to either the natural history of this disorder or to any reasonably expected regression to the mean.

This brings us back to arguably the most important question raised by the Astin study: how should the results of this study be extrapolated to clinical practice? More succinctly, if you are a practicing clinician sitting in the office with a patient, should you recommend that they pursue mindfulness meditation and Qigong movement therapy? Maybe. These data suggest that your patient may derive a benefit from this treatment, especially given that there are limited other therapies that are effective in FM. Alternatively, if there is a robust education, exercise, or cognitive behavioral therapy program available to your FM patient, these and other data suggest that these are treatments worth recommending.

Performing a simple self-examination exercise may also help practicing clinicians put these data in a different perspective. Imagine for a moment that the details of this study were slightly different, and that instead of involving individuals with FM, this study was focused on treating individuals with refractory rheumatoid arthritis (RA). These 2 conditions are probably comparable for purposes of this exercise because they are equally (un)responsive to standard therapies, and the natural history of both conditions is not to spontaneously improve. Imagine also that the interventions were different: the active treatment was a new biologic compound instead of mindfulness meditation and Qigong movement therapy, and the comparator was a tumor necrosis factor- α inhibitor known to be effective in RA, rather than an education program. Finally, imagine that the results of the study were the same as the Astin study: the new treatment performed as well as the active comparator, and achieved both clinical and statistical significance in the primary and secondary outcome measures. Is the glass now half-full, or half-empty?

Our biggest challenge in studying alternative and complementary medicine is not to determine *whether* these interventions work or not. They do. The millions of patients who typically pay out-of-pocket for the plethora of available therapies should provide all the data we need to come to this conclusion⁷. The real issue is *how* and *why* these therapies work in clinical practice, and whether there are specific beneficial effects of these treatments.

If good scientific studies demonstrate that most complementary and alternative therapies are just incredibly effec-

tive “placebos,” then we must understand the crucial elements of the therapeutic encounter that are required to engender these powerful effects. As someone wise once said, being a physician has been a noble profession for centuries, yet we have only had efficacious treatments for decades. We are now reaching the point where we can actually begin to analyze and dissect the psychology and neurobiology of these nonspecific factors that make patients improve^{8,9}. These are exciting times for those of us who feel that the term “placebo effect” has too many different meanings, and that because of this the “placebo” construct is typically in a negative light, rather than the powerful adjunct to therapy that it is. Thus, we need to be careful about being too dismissive of therapies that work well in clinical practice, but that cannot be demonstrated to be better than “placebo” in randomized controlled trials. In caring for complex medical conditions like fibromyalgia, we need all the resources we can muster.

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