Pain, analgesia and placebo

In the early 1950s, a new procedure was developed by surgeons in Texas for alleviation of angina and CAD. The internal mammary artery in the chest sends branches to the myocardium; the surgeons reasoned that more blood could be forced into the heart if the other branches of the internal mammary artery to the chest wall were ligated. Great enthusiasm developed for the operation, with 70% of patients experiencing total relief from their angina. Beecher reports this study in which 100 patients were submitted, without their knowledge, to a sham operation in which the chest was opened, the ribs interrupted, and the wound closed without approaching the internal mammary artery. The patients so operated experienced the same 70% rate of relief as those whose internal mammary artery had been ligated. Many also experienced improvement in the electrocardiogram, in their exercise tolerance and in significant reduction in the use of pain medications.


COMMENT: There are few more striking examples of research in dolorology than this study of placebo effects. The ethics of full disclosure in the 1950s apparently did not deter surgeons from doing these sham procedures on angina patients. Needless to say, this strikingly successful new operation, a precursor to the later development of coronary bypass graft procedures was quickly abandoned. This does remind us that most surgical procedures have never been subjected to double-blind, placebo-controlled randomized crossover research. Most surgical procedures, of course, have not been subjected to this “gold standard” research because surgeons cannot be blinded about what they are doing. The final evaluators of outcomes and the patients involved could both be blinded, but few procedures have been subjected to this approach in research. (See below.)

Osteoarthritis of the knee and the placebo effect

After 10 subjects with knee osteoarthritis gave full informed consent including full knowledge of the possibility and nature of a placebo surgery, three were randomized to a placebo arthroscopy group, three to arthroscopic lavage, and three to standard arthroscopic debridement. The evaluating physicians and the patients remained blinded as to treatment. Patients who underwent the placebo surgery reported decreased frequency, intensity, and duration of knee pain, thought that the procedure was worthwhile and would recommend it to family and friends. There may thus be a significant placebo effect for arthroscopic treatment of osteoarthritis of the knee. The small numbers in this preliminary study precluded a valid statistical analysis, and no conclusions can be drawn regarding the superiority of one treatment over another.


COMMENT: In this small pilot study, final evaluators and patients were both blinded and the small numbers precluded adequate statistical analysis. Nonetheless, significant positive results were seen in the three who submitted to the placebo sham procedure. But stay tuned, see below.

Arthroscopic surgery and placebo

One hundred eighty patients with osteoarthritis of the knee were randomly assigned to receive arthroscopic debridement, arthroscopic lavage, or placebo surgery. Patients in the placebo group received skin incisions and underwent a simulated debridement without insertion of the arthroscope. Patients and assessors of outcome were blinded to the treatment-group assignment. Outcomes were assessed at multiple points over a 24-month period with the use of five self-reported scores – three on scales for pain and two on scales for function – and one objective test of walking and stair climbing. A total of 165 patients completed the trial. At no point did either of the intervention groups report less pain or better function than the placebo group. M scores on the Knee-Specific Pain Scale (range, 0-100, with higher scores indicating more severe pain) were similar in the placebo, lavage, and debridement groups: 48.9, 54.8 and 51.7, respectively, at one year (p=0.14, NS for the comparison between placebo and debridement) and 51.6, 53.7 and 51.4, respectively, at two years (p=0.64 and p=0.96, both NS, respectively). The 95% confidence intervals for the differences between placebo and intervention groups exclude any clinically meaningful difference.


COMMENT: In this controlled trial involving 180 patients with osteoarthritis of the knee, outcomes after arthroscopic lavage or arthroscopic debridement were no better than those after a placebo procedure. Here we have adequate numbers for surgical analysis, and the results echoed the original pilot study in 1996. So what are we to conclude about pain and placebo? The perception of pain has an extremely large subjective component in which one’s belief system plays an enormous role. Medical students are unfortunately not generally taught a lot about the power of suggestion, and the influences of the mind on perceptions—of pain, illness or state of health.

Therapeutic effect of placebo

Placebos can be physical (e.g., a manipulation), pharmacological (e.g., a pill) or psychological (e.g., a conversation). Thirty-two trials were reviewed, involving results of no treatment versus pharmacological, manipulative or psychological placebo interventions. Compared with no treatment, relative risk of an unwanted outcome with placebo was 0.95 (NS). For trials with continuous outcomes, RR of an unexpected beneficial outcome
in placebo was —0.28 (95% CI—0.38 to—0.19); this effect decreased with increasing sample size. The pooled standardized mean difference was —0.36 for trials with subjective outcomes (95% CI—0.47 to—0.25) but not for objective outcomes. In 27 trials involving pain treatment placebo had a beneficial effect of —0.27 (95% CI—0.40 to—0.15), with a reduction in pain intensity of 6.5 mm on a 100-mm visual-analogue scale. The authors found "little evidence in general" that placebos had powerful clinical effects. The authors state "outside the setting of clinical trials, there is no justification for the use of placebos."


COMMENT: Not all authors in the field agree that placebo effects are real. In this meta-analysis, the authors, in spite of denigrating the general effect of placebo, conclude that pain intensity was significantly statistically reduced, a result which would seem to be at odds with their general conclusion. This appears to ignore the fact that there is an inevitable placebo effect in every health professional-patient transaction. Since placebo effects are imbedded in every physician-patient interaction, it would be helpful to understand them and utilize them for better outcomes.

Pain and meditation

Ninety chronic pain patients were assigned in an open trial to either routine traditional care or a 10-week relaxation and stress reduction program. The McGill-Melzack Pain Rating Index, Body Parts Problem Assessment Scale, Body Part Map and other psychological instruments were used to assess stress and psychological status before, during and after the 10-week program. Compared to the traditional care group, significant decreases developed in "present moment pain," inhibition of activity due to pain, symptoms, mood disturbances, negative body image, anxiety and depression (all p<.003). The traditional care group showed no significant improvement.


COMMENT: The use of meditation as an element in chronic pain control is a fairly recent development in pain research. This gives me an opportunity to share my own experience with chronic pain and meditation. On investigation of recent onset of chronic low back pain in my forties, a congenital malformation of my lumbosacral joint came to light. Films revealed a second-degree spondylolisthesis of L5 on S1. My orthopedist, of course, said, "Learn to live with it." My response was to begin taking moderate strength analgesics, and within a year I was requiring stronger medication, which raised the specter of drug habituation with such a long-term condition. I sought a number of treatments, eventually finding that the best two were consistent physical exercise (walking and running), and meditation. Of all the elements in my pain management, meditation has been by far the most significant contributor. While it is possible I am only experiencing a marked placebo effect, the best intervention by far has been my practice of a form of Agni Yoga meditation. If it is only a placebo effect because I believe meditation will help, I do not really care. In truth I started

the meditation practice for other reasons and found the pain relief unexpectedly. The regular practice of meditation did not seem to diminish the pain per se, but it simply did not bother me nearly as much. As I type the copy for this column I am aware of pain whenever I stop to think about it, I find it to be present. The meditation practice has somehow made it possible for me to be much less aware of the pain to the point that it interferes with practically nothing I want to do, including a 27-mile hike last summer on the Cascade Crest trail. Recently I have also had considerable effect of treatments by a skilled practitioner of quantum touch. (See Gordon, Richard, Quantum Touch, Box 852, Santa Cruz, California 95061)

More on pain and meditation

In an open trial, the effects of mindfulness meditation were studied in 250 chronic painpatients, the vast majority of whom were experiencing low back pain, neck pain or headache. The process involved practicing Hatha Yoga in slow meditative fashion emphasizing mindfulness with an awareness of breathing. Instruments used to assess pain at baseline and after 8 weeks included the McGill Melzack Pain Rating Index, Body Parts Problem Assessment Scale, Medical Symptom Checklist and General Severity Index. At the end of training, improvement was highly significant (p<.0001) Follow-up at 2.5 to 48 months found 30-55% greatly improved, 60-72% greatly or moderately improved, 25% no change and 1-15% worse. There was a trend toward weakening in the effectiveness over the 4 years of follow-up.


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COMMENT: This is a second published experience with Mindfulness Meditation by Kabat-Zinn who at the time was at the University of Massachusetts. Meditation focuses attention away from pain. The biochemical results of the state of meditation entrain muscle relaxation and an altered state of awareness—a state of detachment or disidentification from the pain. The founder of the psychological discipline Psychosynthesis, Roberto Assagioli MD, stated it well: "Anything with which we identify will control us; anything from which we disidentify we can control." A cancer patient whom I helped manage through her metastatic bone pain once told me after she had undergone three hypnosis treatments, "Oh yes, I have pain, but it's over there in the chair."

Anginal pain and meditation

Chest pain with normal coronary angiograms is often associated with chronic sympathetic activation, anxiety, and depression, and is resistant to conventional antianginal treatment. In nine women with consistent angina, the practice of transcendental meditation for 3 months b.i.d. significantly improved exercise tolerance, angina episodes, and quality of life. Cunningham C et al. Effects of transcendental meditation on symptoms and electrocardiographic changes in patients with cardiac syndrome X. Am J Cardiol 2000 Mar 1; 85(5):653-5. A10

COMMENT: Again, this small pilot study involved such a small number of patients that a statistical analysis was not feasible, and one looks for larger studies with the same design. Even so, here is a common form of chronic pain, that of angina from coronary insufficiency, which can in many patients be better managed with mind-body techniques. They are, of course, not a substitute in dealing with the cause of the angina, but an amazingly appropriate ancillary management approach.

Rheumatoid arthritis pain and prayer

Forty-four adult patients with rheumatoid arthritis were recruited for the study if they met American College of Rheumatology criteria for diagnosis of class II disease, had a positive rheumatoid factor, or had radiological evidence of joint erosions. All subjects had a rheumatological evaluation by a single reviewer at baseline. Subjects underwent a 3-day protocol of educational sessions (6 hours) regarding physical, emotional and spiritual healing, forgiveness, anger, and impediments to healing; and six hours of "soaking prayer" with laying on of hands over affected joints by praying ministers. The first 26 subjects were assigned to a six-month program of daily supplemental intercessory daily prayers for at least 10 minutes by two remotely located ministers. The praying ministers received a picture and brief description of demographic and clinical information regarding the patient to whom they were assigned. The next 15 enrollees were assigned to a waiting list. All underwent re-evaluations of clinical status at 3, 6, 9 and 12 months beyond baseline. Baseline evaluation was compared to interval and final evaluations regarding 10 variables. Four of 44 subjects failed to complete the protocol. Standard rheumatoid arthritis medical treatment was continued. No differences emerged for the waiting list and supplemental prayer groups. All subjects undergoing the initial 3 day protocol experienced increased grip strength (p=0.039), reduction in number of tender joints (p<0.001, swollen joints (p<0.0001), pain (p=0.004), fatigue (p=0.007), and level of functional impairment (p=0.0002).


COMMENT: Intensive prolonged prayers with laying on of hands led to significant improvement in objective and functional measures of these rheumatoid arthritis patients; additional remote prayer did not enhance results. The vagaries of the demonstrated therapeutic effects of prayer are not fully understood. In this study, the beneficial effects can be largely explained on a psychological basis. In other studies in which demonstrable remote prayer effects are found, one must postulate a mechanism that transcends conventional teaching regarding the effects of energy. A common postulation for these non-local effects may lie in the concept of a "collective unconscious" postulated by the two deceased European psychiatrists Roberto Assagioli and Carl Jung.

Low back pain and hypnosis

Fifteen adults 18-43 years of age with chronic low back pain (mean duration 4 years) were found to be moderately/highly hypnotizable based on the modified 11-point Stanford Hypnotic Susceptibility Scale. Somatosensory event-related potential correlates of noxious electrical stimulation were evaluated during attend (control) and hypnotic analgesia conditions at anterior frontal, midfrontal, central, and parietal regions. Significant brain inhibitory processing was evidenced in different brain locations (p<.05-p<.001) compared to the control condition. Hypnotic analgesia led to highly significant mean reductions in perceived sensory pain and distress (p<.001). Participants were then shown to develop self-efficacy through the successful transfer of newly learned skills of experimental pain reduction to reduction of their own chronic pain; within three sessions, they reported chronic pain reduction, increased psychological well-being, and increased sleep quality. In 60% the pain was totally gone and in 80% the distress was totally gone by the end of the third session.


COMMENT: Hypnotic analgesia is an active process that requires inhibitory effort, dissociated from conscious awareness, in which the anterior frontal cortex participates in a topographically specific inhibitory feedback circuit that cooperates in the allocation of thalamocortical activities. The development of "neurosignatures of pain" can influence subsequent pain experiences, and may be expanded in size and easily reactivated. Therefore, hypnosis and other psychological interventions need to be introduced early as adjuncts in medical treatments for onset pain before the development of chronic pain. These techniques are enormously successful and are grossly underused, probably because they are not adequately or commonly taught in medical education systems. Pain is, after all, perhaps the most common reason for admission to hospitals. One cannot think of a single intervention that could more significantly impact the cost and inconvenience of overuse of hospitals.

Robert Anderson is a retired family physician. In mid-career, his practice took a holistic turn as decades passed. He has authored five major books, Stress Power!, Wellness Medicine, The Complete Self-Care Guide to Holistic Medicine (co-author), Clinician's Guide to Holistic Medicine (McGraw Hill, 2001), and The Scientific Basis for Holistic Medicine, (6th edition 2004), now available from American Health Press, holos@nwi.net. Anderson was the founding president of the American Board of Holistic Medicine, past president of the AHMA, former Assistant Clinical Professor of Family Medicine at the University of Washington and currently Adjunct Instructor in Family Medicine at Bastyr University.

LETTER for DOCTORS & PATIENTS - JANUARY 2005

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