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Placebo: “I shall please”– Vespers of the Dead

The meaning of the Latin word placebo has undergone a long metamorphosis from its medieval use (above) and its somewhat ambivalent use today. Before the advent of evidence-based medicine physicians were known to employ sugar pills or other harmless nostrums as treatment. They sensed intuitively that the giving of medicine helped ill people feel better. Little thought was given whether these conferred actual benefit or as Voltaire put it “amused the patient until he got well.” Thomas Jefferson justified placebos as “a pious fraud.” Because of the implied deceit and an increasingly informed populace this manifest use of placebos has fallen into disrepute. Physicians and pharmacists no longer secrete sugar pills in their desk drawer. Meanwhile, the term placebo has been applied to the dummy medication or procedures used as the controls for clinical trials of proposed treatments. This is unfortunate since such controls embrace no deceit and the consenting subjects are informed. Any thoughts about placebos must comprehend these subtle distinctions.

The Placebo Effect

A placebo is commonly thought of as a thing; that is a pill, a device, a procedure that is employed by a healer to help or seem to help his or her patient. It is more instructive to think of it as an effect: the effect of a treatment that goes beyond its intended pharmacological or physiological effect. It is said that the history of medical treatment is the history of the placebo effect, for most medical treatments employed before the first third of the last century are now known to be ineffective. Modern clinical trials provide the scientific base for much of what doctors do. Nevertheless, alternate therapy and much of conventional medicine must rely on the placebo effect since in many situations there are few tested options and the process of gathering scientific evidence of efficacy is laborious and incomplete. Before we explore the placebo effect further, two other terms require explanation: the nocebo effect and the natural history of the disease.

The Nocebo Effect, “I shall not please”

A treatment administered by a healer may have a bad effect. Of course any treatment may have a predictable risk of untoward effects. The nocebo effect denotes worsening

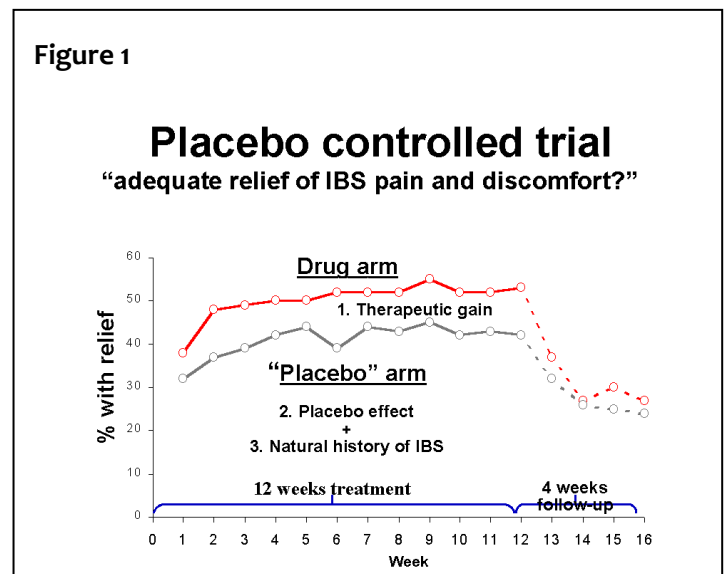
beyond this predictable risk. All communities have had powerful individuals who through the force of their station and personality have the power to do people good or ill. Voodoo, witch doctors and priests hold exalted positions in societies primitive and advanced, and doctors often fill the role in ours. Willful or careless, a healer might harm a patient through an unsatisfactory relationship.

Natural History of Disease

Natural history is what would happen to a patient if there were no treatment intervention. An ill person if left alone will usually improve. A cold lasts a week if treated, 7 days if not. The progression of diseases varies greatly. The course of cancer may be downhill, while that of high blood pressure may be static over long periods. Chronic, painful conditions such as the irritable bowel syndrome (IBS) and most of the other functional gastrointestinal disorders tend to fluctuate greatly, not only in severity, but also in the predominant symptom. Natural history like the placebo effect must be taken into account if we are to understand the usefulness of any treatment.

Placebo Effect and Clinical Trials

Figure 1 illustrates a modern randomized, double-blind, placebo-controlled clinical trial of a drug for the treatment of IBS. Such trials are the bedrock of evidence-based medicine.



They provide the scientific basis of rational therapy that permits doctors to make therapeutic decisions that help most patients who fit the conditions of the trials.

The three central features of such a trial are; (1) that all entered subjects have a similar illness and are equally likely to fall in the control or treatment groups, (2) that the endpoint or measure of treatment success is decided in advance, and (3) that all engaged parties are unaware (blinded) as to whether an individual subject is receiving the drug to be tested or an inert replica, the so-called placebo. In the study illustrated in figure 1, all the entered subjects had IBS without constipation and weekly recorded whether they had achieved “adequate relief of IBS pain or discomfort.” From the illustration, it can be seen that during the treatment period the drug achieved a greater improvement than the placebo and the difference between the two is called the therapeutic gain. Without this difference, it would be concluded that the drug has no (beneficial) effect.

However, in most of the treatment group and the entire placebo group improvement was apparently not due to the drug. This effect has erroneously been called the “placebo response,” but there are two components, the placebo effect and the natural history of the disease. Since IBS fluctuates, some patients would have improved with no treatment at all. In the figure notice that the benefit falls when the drug is stopped, but not to zero (-0-). Also notice the decline in benefit to a similar level when the placebo is stopped. It is impossible to say from such a study how much of this non-drug improvement was due to natural history and how much to the benefit of the therapeutic encounter.

Placebo Facts

For such an important medical activity, it is surprising how little we know about the placebo effect. However, there are some clues albeit scattered and sketchy. For example, an injection of an inert substance has a greater effect than an inert pill. Large pills are more effective than small pills, and certain colored pills enhance sedative or simulative effects. A medication given by a doctor has a greater effect than that administered by a nurse, and the placebo effect is least if the pills are delivered in the mail. Pain relief lasts longer if a placebo is substituted than if the painkiller is simply stopped. There is no such thing as a “placebo responder.” All of us respond differently at different times and to different exposures to placebos. The intelligent and the educated are as susceptible as others are, but some experts think that “analytical thinking” can mitigate the response. Thus not only is what is given important, but also when, where, by whom and how. The healer-patient relationship is key.

Components of the Placebo Response

From the foregoing, one would think that the study of the placebo effect and how to maximize it would be fertile subjects for research and medical school teaching. Alas this is not the case. However, we do have some ideas of how this essential benefit occurs.

We think of pain as a sensory phenomenon transmitted like a telephone message by nerves. However, there are many other influences on how we perceive pain such as attention, fear and anxiety. Healers who are able to relieve the fear and anxiety can make a patient feel better. I participated in a study where half the IBS patients seeing their family doctor secretly feared cancer. Most of these left the doctor unrelieved of this burden and an opportunity to relieve the fear and anxiety was lost. Perhaps also, like Pavlov’s dog, we are conditioned to feel better when we see a doctor. Previous experience, likely as a child, reinforces the healing experience. Moreover, if we expect and desire to feel better on a treatment we are more likely to do so. A healer is often in a position to give meaning to a person’s symptoms in the form of a diagnosis. A diagnosis, even if it is of a little understood illness, helps make suffering understandable. We cope better when we know the enemy.

It seems to this writer that the most important actor other than the patient is the healer. Educated, experienced, wise and caring, a doctor should be able to establish a powerful relationship with a patient to maximize a therapeutic outcome. In a sense, the doctor is the placebo. Whatever the outside influences, healer and ill person have a contract, or a relationship that should in itself be therapeutic. All of us in health care: professionals, payers, administrators and patients should strive to preserve, understand, and nurture this ancient human relationship.

Conclusion

A placebo is an effect, not merely a thing. It is more or less a component of all healing yet is poorly understood or studied. In clinical trials a placebo pill, device or procedure acts as a control to ensure that the effect seen with the treatment is specific, and not only the result of the placebo effect or the natural evolution of an illness that accompany every therapeutic encounter. The importance of these effects is emphasized by nocebo encounters, too many of which we read about in the press. These often involve failure of the therapeutic relationship. In the absence of more knowledge, we must strive for conditions that tend to maximize the benefit: relief of anxiety, education, firm diagnosis, caring, and above all a satisfactory doctor-patient relationship.

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