

EDITORIAL

PLACEBO

I don't recall the term "placebo" being used during my undergraduate or optometric educations. Nevertheless, I was aware that it did exist primarily as the "sugar pill" dispensed by one or another country doctor. This was the case in movies I had seen at one time or another. And it always brought great relief to the patients.

My first more substantial encounter came about in the 1980's during a course in pharmacology that was required to extend my license to the use of diagnostic pharmaceutical agents. The instructor was discussing the process by which drugs are tested to obtain FDA approval. He covered double blind controlled studies at some length. I was astonished when he then stated that there was ample proof, not just evidence, that an average of 30% of the control or placebo treatment groups experienced the same beneficial effects as those who actually received the drug being tested. To this day I believe that although this information was given as an aside, it was one of the more important things I learned in that course.

During the 1990's there was an increasing number of articles in the popular press that did in-depth reporting on medications. Most served to bring about a public awareness that there were frequently significant side effects and that patients should actively question their health care providers about medications being prescribed. One such article reported a review of 45 studies on several antidepressants. This was particularly interesting to me for two reasons: a number of my patients were taking this class of medication, and the article discussed placebo.

"The researchers who obtained the information from the Food and Drug Administration through a request under the Freedom of Information Act, found that 40.7% of patients in the trials who received the drugs showed a reduction in symptoms, compared with 30.9% of patients who received placebos."¹

It is not unusual for results of studies to be reported in this manner in peer reviewed journals, magazines, and newspapers. And while the almost 10% difference in favor of the antidepressants appears impressive at first glance, something bothered me. Consequently, I've raised the following question a number of times with people who are expert in research design and interpretation: how is the placebo effect accounted for in the experimental group? In the example above, I assume that the experimental and placebo(or control) groups were matched as closely as possible in all variables. So, if 30.9% of the control group benefitted from the placebo, is it not possible that the same effect was present in the experimental group? In other words, could the drug under investigation be a placebo for some in the experimental group? This could potentially reduce the efficacy of the drug from 40.7% to 9.8%.

I've not received an answer to the contrary. However, at least two people who are well versed in research methodology stated that the next step in interpretation is to determine statistical significance. But, statistical significance deals with chance and not specifically the placebo. Both agreed that it is not clear that these two entities are the same thing or that the one subsumes the other.

This question became an impetus to learn more about placebos. A Medline literature search revealed a plethora of articles on the topic. An admittedly less than exhaustive reading of these works has brought about an understanding that placebos are complex and presently a subject of considerable research and speculation. Nevertheless, several things are certainly worth stating.

It is productive to distinguish between the placebo and the placebo effect. Although there is not universal agreement on the exact characteristics of this distinction, I propose the following: a placebo is a therapy that is administered with or without the knowledge that it is minimally or not at all effective in treating a particular condition. The placebo effect is the psychological or psychophysiological beneficial consequence of the placebo in terms of ameliorating the condition.² Thus, the placebo can be given to the patient in the belief that it will work, or with full awareness that it is a "sham" treatment. This is fairly straight forward. On the other hand, the placebo effect is more complex.

A reasonable starting point to understand the placebo effect is to determine its mechanisms. The above definition's inclusion of psychophysiological aspects is a recognition of research that has been reported in this regard. Quite interestingly there is evidence that the placebo effect is present even when "hard" or objective clinical endpoints are measured. In reviewing this literature, Margo states that the placebo effect was evident in such objective clinical endpoints as blood pressure, heart rate, exercise tolerance, peripheral blood flow, serum hormone concentration and elements of the

cardiogram. He also reports that, on a biological level, studies with laboratory rats have shown they can be immunosuppressed with saccharin water.³ Thus, the “sugar pill” has been shown to have physiological and biological effects.

Nevertheless, the placebo is a strong component of acceptable research. It is not only part of the gold standard of investigating the effects of introducing a foreign substance into the body, but it is also considered to be essential in investigating the effects of non-invasive interventions such as vision therapy. Yet, the same question still remains: how is the placebo effect accounted for in the experimental group? Still, sound research requires us to consider the placebo: it is the best device we presently have in seeking the truth, even though it is probably imperfect and not completely understood.

Aside from the research aspects of placebo, there is another dimension the literature addresses. This relates more to clinical aspects; the health care provider him or herself as a “walking placebo.”^{2,4} The mechanisms here for the placebo effect are not presently explained on physiological or biological levels, but more anthropologically: they are said to be versed in cultural and societal symbolisms and expectations.⁵ This concept brings to mind conversations I’ve had with a number of optometric students and residents over the years. The point was always to have me explain how two optometrists could prescribe the same intervention for the same condition in patients whose histories and findings were similar, and obtain vastly different results. I gave explanations that never truly satisfied the questioners or me, but I never raised the possibility of a placebo effect.

It is impossible to deny that the placebo and the placebo effect are a part of health care in both its provision and research. Yet, they are usually not openly discussed, except in a negative manner. As long as we view them as an embarrassment in providing health care and as an annoying enigma in research, we do ourselves and our patients a disservice.

References

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