Placebo and Placebo Effects: Practical Considerations, Ethical Concerns

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Case scenarios are written to express typical situations that family physicians may encounter; authors remain anonymous.

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Case Scenario

I have several patients who have irritable bowel syndrome (IBS), and I frequently give them acidophilus supplements, which have been shown to help some patients with gastrointestinal problems, although their use in IBS has not specifically been supported or denied. More than one of these patients has come back saying that I was a terrific doctor because they experienced considerable relief from the supplements. Frankly, I think the supplements are not much better than a placebo. Similarly, I will tell patients to use over-the-counter vitamin supplements. When my patients ask if I believe that acidophilus or vitamins work, I reply, "They work in some people; you've got to allow a few days to see if they'll work for you." I know that placebo can be a powerful remedy, and I do not think I am doing any harm. Are these supplements placebos? Do patients always have to be told that something they are using is a placebo? If so, how? Or, if not always, where do we draw the line?

Commentary

First, it is important to define what is meant by "placebo". Strictly, the term placebo, taken from the Latin "I shall please," refers to any intervention, event, or experience that evokes positive subjective or objective outcomes in a patient (or research participant). A pure placebo is an agent that has no known physiologic effects, whereas an impure placebo is a substance that has some biochemical properties, but these are irrelevant to, or ineffectual in, the clinical circumstances in which the substance is being used.[1] In the present case, both acidophilus and vitamin supplements would not ordinarily be considered to evoke any direct, pharmacologically therapeutic effect against the symptoms of IBS. However, these supplements may be impure placebos.

IBS is a disorder of somewhat heterogeneous etiology that may be neurally, hormonally, and/or immunologically mediated, and affected by psychological variables.[2] It may be that a generalized improvement in digestive function (as might be produced by acidophilus) or the provision of certain neural or immunologic cofactors (via vitamin supplementation) may afford clinically relevant, albeit subtle, benefits. In addition, these agents might be serving another purpose; by engaging and accommodating patients' expectations and reinforcing the physician's perceived therapeutic role, the clinical encounter and rendering of "treatment" may evoke positive subjective (e.g., cognitive) and objective (e.g., physiological) effects.

The two major practical harms incurred by the use of inert agents to evoke a placebo effect are the risk of improper treatment and the expansion of this practice to the extent that patients may then employ the agent in inappropriate circumstances.[3] In the first instance, it is particularly important to consider that impure placebos may exert some biochemical actions that could produce adverse effects in some patients. In the second instance, problems can arise when patients use such agents excessively or for conditions that warrant other available interventions.

We also need to understand placebo effects as neurophysiologic responses that arise from expectations.[4] It is becoming increasingly apparent that a patient's state of mind can affect, if not determine, clinical outcomes. Physicians should appreciate patients' subjective experiences and interpretations

of illness and the clinical encounter, and understand how these factors may contribute to neurophysiologic mechanisms underlying the placebo effect.[5,6]

Although we tend to think of such effects in terms of positive outcomes, it is important to recognize that patients' negative or unmet expectations (including those arising from adverse experiences within the clinical environment) can also incur strong conditioning and physiologic responses. These responses can increase signs and symptoms of disease and subjective illness and are known as nocebo effects (literally meaning "I shall harm").[7]

Knowing that a particular treatment—however inert—*can* evoke mechanisms to produce positive outcomes does not mean that it *should* be used. The covert use of placebos leads to unavoidable ethical harms. By not informing the patient about the nature of the treatment, the physician is being intentionally deceptive and therefore undermining the truth-telling that is critical to trust within the physician-patient relationship.[8,9] Deception within the medical relationship creates an overt paternalism that harms patients by denying the patient the information necessary to provide an informed consent to be treated and by suppressing the patient's right to refuse particular treatments (i.e., the "negative right" of autonomy). Moreover, revealing such deception could irreparably damage patients' trust in the present medical relationship and the medical system in general.[10]

This prompts considerations of: (1) whether patients must be informed of the use of a placebo; (2) if such disclosure negates the placebo effect; and (3) if and how a placebo or the placebo effect might be ethically utilized in clinical practice. Interestingly, it has been shown that disclosing that an agent may have negligible therapeutic value may not necessarily reduce its potential to evoke placebo effects, as long as the circumstances in which this information is provided afford a sufficiently positive reinforcing value for patients' expectations of the clinical encounter.[11] Although we strive toward as much clinical certainty as possible, medicine remains a somewhat uncertain practice; communicating this uncertainty by conjoining it to optimism allows for truthfulness and intellectual honesty, while still fostering trust and sustaining hope.[12]

Knowing where to draw the line is actually quite simple: do not lie. Although there are no hard and fast rules, it has been suggested that the use of inert agents to evoke placebo responses should adhere to certain guidelines. Using the placebo effect in the clinical setting is only acceptable when the following conditions have been met: (1) there is a well-established, durable physician-patient relationship; (2) there is a concrete diagnosis that does not mandate or support the use of other, "active" interventions; (3) the patient specifically requests that the physician provide some form of intervention; (4) the use of such agents is a consideration of last resort; and (5) the use of such agents does not substitute for, or interfere with, diagnostic and therapeutic diligence.[13] In these instances, a physician might explain that even though a particular agent or treatment has not been shown to have any specifically therapeutic properties, it may engage mechanisms that, in some ways, can reduce feelings of illness and perhaps evoke physiological recuperative processes.[14]

Regarding our clinical scenario, it might be appropriate to state that acidophilus and vitamins may work in some instances, adding that, "Although they may not directly affect your IBS, they may turn on other mechanisms that might be important for your health and might make you feel better." This could meet the patient's expectations and incur a positive conditioning response to the clinical encounter.

Knowing whether a particular patient will be receptive to this information, knowing how to phrase such information and how much information is required, and prudently discerning whether placebo effects are viable in a specific patient requires a good physician-patient relationship. To be sure, the nature and depth of this relationship determine the scope, tenor, and context of the clinical encounter, and, like any relationship, each will be different.[15] Despite the pressures incurred by the contemporary health care system, it is wise to remember that the practice of medicine involves the focus of scientific knowledge upon the

humanistic endeavor of curing, healing, and caring. Creating a positive therapeutic environment that acknowledges patients' expectations and sustains trust and hope is a foundation of medicine's human dimension. Perhaps the best placebo effects are not gained from the use of inert agents, but are derived from the power of the clinical encounter itself. To paraphrase Brody[1] and Spiro[16], the placebo effect should begin when the physician enters the patient's room.

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