The Paradoxical Placebo

Mary Rorty
Lorry Frankel

Abstract

We instance a clinical case where use of an inert placebo furthered an important clinical goal--diagnosis. We consider this use in light of common objections to the use of placebos in clinical practice and question whether this use of a placebo is subject to those objections. We note that the use made of placebo in this case falls under the letter of the prohibition in the AMA Opinion, although qualified in their accompanying report. We agree with Dr. Foddy that "if placebos are to be used clinically, they must be used deceptively." Because informing the patient that a placebo is in play makes a diagnosis less likely, we conclude that the hope for a useful non-deceptive use of the intrinsically deceptive placebo is admirable but possibly futile. Since a placebo is only effective if it is not identified as such, to require that placebo be used only if disclosed is tantamount to suggesting that it never be used except in drug trials.

The Paradoxical Placebo

Introduction

The problem is a simple one. A placebo is "a substance provided to a patient that the physician believes has no specific pharmacological effect upon the condition being treated."[1] But it is delivered in the context of medical treatment. The paradox of the placebo is that its efficacy, if it has any, depends upon the belief of the patient that the offered treatment is appropriate to the presenting condition. But it seems contrary to the spirit of contemporary medical practice to deceive patients. Placebos given in the context of medical treatment are essentially deceptive. If deception has no place in clinical medicine, placebos, it seems, have no place in the treatment of patients.

Dr. Foddy[2] suggests that prescription of placebos "within ethical limits" may further appropriate clinical goals without imperiling patient autonomy, and without damaging the trust that is crucial to a therapeutic relationship between physician and patient. We agree. Although undisclosed administration of placebos flies in the face of the general prohibition against deception in medical practice, that is not sufficient to disqualify the practice. Ethical use of placebos is possible independent of whether they are disclosed or not, unless it can be shown that the practice harms the patient.

The article speaks primarily of the use of placebos in treatment. We agree with our author that "if placebos are to be used clinically, they must be used deceptively," in order to be effective. "If patient expectations can control the magnitude of the placebo

effect, the AMA[3] is just wrong when it suggests that doctors can reveal the inert nature of the placebo…without compromising their efficacy."

We wish to address a parallel context for using placebos in clinical practice. In a case recently brought before an ethics committee, the use of a placebo in diagnosis raised the question of whether a patient was being inappropriately deceived. We consider the intention of the intervention and its consequences to be relevant to its ethical valence, and question whether deception alone is sufficient to render a treatment inappropriate.

The case

An adolescent woman born with a congenital heart deformation (left transposition of the great arteries) is being evaluated for the timing and value of a heart transplant—a high-risk procedure with long term consequences. She suffers from parasthesis of her lower extremities, migraines, enuresis and transient neuropenia.. She is perceived to suffer from anxiety, is hypersensitive to changes in her body, and very anxious about exerting herself.

In order to determine whether transplantation is appropriate at this time, the attending physician suggests that for a given period of time she be given a blinded trial of heart medicine (milrinone) or an inert placebo—normal saline. If the symptoms improve to the same extent with normal saline as with the milrinone, it will confirm that psychological factors compound her degree of disability, and thus her self-report of symptoms cannot be relied upon in determining the best timing of her next stage of treatment.

Normal saline is a placebo in the purest sense: pharmacologically inert—not, as in some of the cases in the literature, a sub-optimal pharmaceutical alternative to the 'best' treatment, nor (as in a case mentioned by Foddy) a sub-optimal dose of an effective medication. There is no intention to "mollify the patient for the convenience of the physician." The purpose of the placebo is to aid in determining what course of future treatment is in the best interests of this patient at this moment.

There are two possible outcomes, either of which could serve the patient's best interests. The reported symptoms may be shown by the trial to be entirely physiological in origin, and thus accurately discriminatory of the state of the patient's heart. Alternatively, there may be enough psychosocial influence on her present condition to suggest the need for postponement of or further preparation for the serious intervention that a heart transplant represents. The trial which is being suggested may contribute important information to the decision .

Deception in clinical medicine

The most frequently cited reasons for suspicion of deception in clinical medicine are threats to the safety or autonomy of the patient, and possible damage to the trust so central to a therapeutic relation between the physician and patient.

Safety

Safety is of course an important consideration. There is a wide range of options considered as 'placebos' in the literature, including complementary and alternative medicines (the effects of which have for the most part not been subjected to research, and so are clinically uncertain) and various 'inpure' placebos—antibiotics, acetominaphen,

vitamin pills, or suboptimal doses of pharmaceutically effective medications, when used in amounts or for conditions for which they are ineffective. The placebo in our case is a 'pure' placebo, unlikely to constitute an independent risk in its own right.

Autonomy

In our case, is the patient's autonomy being disrespected? Is alternating the administration of a heart medicine with a neutral placebo a threat or challenge to the patient's right of self-determination? She is there for, and has agreed to, an evaluation—a decision about whether a serious intervention is appropriate. If she does not wish to be considered for a transplant, she can decide against undergoing the procedure even if it is determined to be appropriate in her case. The information potentially available from the intervention may be important for her ability to decide whether to agree to (or refuse) the intervention. If her fear of or ambivalence about the operation is a complicating factor in her evaluation, it may imperil the success of the outcome of the procedure, and needs to be appropriately addressed before proceeding. It may signal the need for further psychological evaluation, or for information additional to that already provided. All these exercises of self-determination are furthered by the information derivable from the suggested intervention.

Patient's best interests: Is the individual being "instrumentalized" in this intervention, treated as a means, rather than as an end in herself? Is something other than her medical best interests at stake? Both the necessity for, and the potential effectiveness of, the proposed intervention are very much at the forefront of consideration in the case as described. The patient's interests are not being subordinated to, or ignored for the sake of, any larger research interest or competing third party interests. The historical instances

that lie in the background of our contemporary concern for avoiding deception in medicine—the Tuskegee syphilis study or the radiation research of the 1950s—are not in in any way analogous to this case.

Trust

What about possible damage to the physician patient relationship, and the trust that is so important for that relationship? The patient has sought out the physician for an evaluation, and the information that may be derived from the placebo trial could be an important part of that evaluation. It is not clear that the patient's trust, or her reasonable expectation of an honest, fair and informed decision, is in any danger.

The AMA and clinical use of placebos

Much of the literature on clinical uses of placebos deal with a different kind of case. The harassed pediatrician succumbs to patient pressure and prescribes an antibiotic for a virus, even though believing that there will be no appropriate pharmaceutical effect. Dr. House pockets the hydrocodone from the vial and replaces them with breath mints for the patient with inconsistent symptoms (with such success that he gets a request for a refill). The case we describe, however, seems quite different. It is not the doctor's convenience that is involved in this diagnostic context.

But the use of placebo in diagnostic, as well as therapeutic, contexts is explicitly included in the 2006 AMA Opinion on the use of placebos in clinical practice: "Physicians may use placebos *for diagnosis* or treatment only if the patient is informed of and agrees to its use." (author's emphasis) Regardless of whether diagnosis or treatment

is at stake, disclosure of the use of placebos seems to be required by the AMA recommendation.

Research or treatment?

The use of placebos in double-blinded trials in research has become institutionalized as an important strategy for drug development, and may be one of the best, if not only, routes to approval for a drug. Informed consent for participation in a research protocol typically includes explicit discussion of the role of placebos as an alternative to treatment in drug approval. Our case presents use of a placebo in a medically controlled, clinical context.

An article accompanying the release of the AMA Opinion 8.083 (Bostick et al, 2008) makes specific reference to situations such as those in our case, single patient controlled studies, sometimes known as 'n-of-1 trials' (Irwig et al 1995).. This is explicitly described as a case where the placebo should be used 'without relying on deception' and best addressed in the context of 'shared decision making'—which seems to amount to telling the patient that among the medicines that will be tried in evaluating her illness some will be 'not pharmacologically active.' The 'n-of-1 trial' is either a special case of clinical trial, according to some sources (Louhiala 2009, 409) and thus more appropriately considered research than treatment—or a purely clinical procedure, useful in the context of diagnosis in a thoroughly non-research calculation of best treatment for an individual patient. Does the way it is described determine the rules that govern it, the kind of consent document the patient must sign?

So, what is a placebo, anyway?

There has been a flurry of empirical research on placebo use in clinical contexts. When questioned, large numbers of physicians report using placebos in non-research clinical practice (Sherman & Hickner 2008, Louhiala 2009). This suggests that there is *prima facie* reason to believe that many physicians achieve results that they consider desirable from their utilization. But however narrow its use in its latin origin, the term 'placebo' is now so thoroughly integrated into ordinary language that a variety of substances, and of uses and effects of those substances, are encompassed under the term. To survey placebo use without greater specification is to inquire indiscriminately into (a) the substance being used; (b) the physician's intentions, and (c) the effect of the substance, whatever it is, on the recipient, whatever the physician's intention—the so-called 'placebo effect.'[7]

Failing to distinguish between 'pure' (=pharmacologically inert, and so probably harmless) and 'impure' placebo—drugs or other therapeutic modalities used without adequate reason to suspect they might be useful—serves only to cast the term in quite unnecessary disrepute, since actual harm might result from the latter. We recommend the term be used only for the former, and describe the latter as either bad choice of therapy, or lack of adequate information.[8] Certainly there are abuses of physicians' intentions—it may be that there have been occasional circumstances when a physician has intentionally deceived a patient by describing as therapy something which is known for sure to be useless for the condition presented; but although it may be such failures of professional practice that the AMA policy is directed toward, it seems unfair to assume that such cases of explicit deception are anything but rare. Finally, the 'placebo effect'—whatever its complex biopsychosocial explanation may be—seems quite independent of either the nature of the substance being used, or the physicians intentions, but rather a serendipitous

side-effect of normal clinical practice that, when present, may be admired, or deplored—but probably not controlled.[9]

Deception and disclosure

Even setting intentional deception aside, there are practical problems embedded in the suggestion that all placebo use be disclosed to patients—problems that are rooted in what we have called the 'paradoxical nature' of the placebo itself. A placebo, in order to merit the name, is by definition deceptive. It is not a treatment—it has 'no specific pharmaceutical effect on the condition being treated.' It may have some utility, whether therapeutic, as some argue, via the universally admired 'placebo effect,' or diagnostic, as in the case we describe—if, and only if, you, the patient, do not know that it is not a treatment for your condition. To what effect, then, is disclosure? And if, as the AMA urges, disclosure is nonetheless obligatory, when, and how, should the disclosure that is being recommended be made? When you enter the hospital, as part of normal admission procedure? When you first meet your physician? When the decision is made to embark upon a particular stage of an ongoing and longitudinal evaluation process? When the IV is being set up to administer the alternatives?

The increasing scrutiny and qualification surrounding clinical uses of placebo, through the recent AMA Opinion as well as comparable elaborations by the World Medical Association, [10] reflect the emphasis on patient autonomy and informed consent in current medical practice. The insistence on disclosure represents an imposition of expectations appropriate to research on clinical practice contexts. By insisting on

disclosure 'within the context of shared decision making,' physician discretion about what, and how, to disclose within an ongoing therapeutic relationship is diminished.

Conclusion

If I tell you that among the measures to be taken to determine the nature and severity of your illness are some that are known to be, and intended to be, ineffectual, it is quite possible (and some would say even inevitable) that your trust in me as a physician—the trust that I had hoped, by my honest disclosure, to maintain—might in fact be undermined, rather than strengthened. If placebos are to be forbidden in clinical medicine, the use of a placebo in this diagnostic context is called into question, despite its obvious utility.

The placebo is only effective insofar as it is deceptive. The hope that there can be non-deceptive uses that serve its purpose is conceptually confused at best, and likely futile.

---

[1] This definition is from the AMA Opinion on Clinical Use of Placebos. It is in one sense too narrow (it does not include non-pharmacological agents which might nonetheless be used as placebos) and another too broad (it does not distinguish between pharmacologically inert, or 'pure' placebos, and pharmacologically active or 'impure' placebos). In the article on which we are commenting Dr. Foddy seems to presume placebos are typically inert, but not necessarily pharmacological.

[2] Foddy B A Duty to Deceive. AJOB x (y) pp.

[3] AMA Code of Medical Ethics: Current opinions with annotations, Opinion 8.083.

[7] Thus in a recent article (Louhiala 2009) the author notes that in some recent empirical studies on placebo, "(b)ecause the key concept was not defined, the respondents may have understood placebo in at least four different ways. First, …deliberate deception through the administration of an intert substance. Second, it may have meant giving an intert substance openly…Third, …a situation in which the doctor or nurse believes that the drug works, even though there is no supporting scientific evidence. Fourth, some respondents may have thought more about the placebo effect than the nature of the substance given." (p.407)

[8] In the literature, for instance, there is some tendency to subsume some complementary or alternative therapeutic modalities (CAM) under the heading of 'placebo,' although others argue that they respresent insufficiently researched therapies, rather than intrinsically deceptive therapies.

[9] The AMA opinion expresses the hope that despite disclosure of the use of placebos, the 'placebo effect' can still be achieved in clinical medicine—probably a vain hope.. An additional paradox of the placebo,

which is not discussed at length in our commentary, is that an actual placebo is neither necessary nor sufficient for the 'effect.'

References

Bostick NA, Sade R, Levine MA, Stewart Jr DM (2008): Placebo Use in Clinical Practice: Report of the American Medical Association Council on Ethical and Judicial Affairs. *Journal of Clinical Ethics 19*(1) 52-61.

Hrobjartsson A (2008) Clinical Placebo Interventions are Unethical, Unnecessary and Unprofessional. *Journal of Clinic Ethics 19*(1) 66-69.

Louhiala P (2009): The ethics of the placebo in clinical practice revisited. *Journal of Medical Ethics 35*, 407-409.

Louhiala P (2008): Rethinking the placebo effect. *Medical Humanities 34,* 107-109.

Smoak Jr R (2004) Placebo: Its Action and Place in Health Research Today. *Science and Engineering Ethics 10* (1) 9-13