

## Ethical Analysis of Placebo Testing: *Clinical Trials vs. Clinical Treatment*

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Over the course of the century a new issue in modern medicine has arose and paved the way for most ethical debates today. The issue society is faced with is the implementing of placebo testing and when, if ever, that method is appropriate. The term placebo as used in this paper will carry two separate meanings that will become clear in the explanation of clinical trials and clinical treatment. Numerous articles have been published as of late giving opinionative answers to the dilemma of placebo testing; however, by researching specific experiments and articles I have shown that clinical treatment of patients is the only place for the utilization of placebo in today's practice. This paper will show various methods of testing involving placebos and I will give evidence to the immorality of placebo testing in the quest to improve the ethics of modern medicine. A topic as diverse as this will have various exceptions to the rule; however, the end result will show the impact of ethics, morality and fairness of choosing placebos in a proper way only to be used in clinical treatment, as opposed to clinical trials.

Due to complex nature of a medical issue such as this, it is crucial to understand the basic principles and history of the controversy before any sort of analyzing begins. The placebo is an inert substance that carries no pharmacological activity. It processes the same qualities as the drug that is being compared such as the same taste, smell, and appearance. However, placebos are not strictly pharmaceutical; many placebos are utilized in sham surgeries. A placebo surgery is conducted as if the patient would be undergoing a legitimate surgery. The patient is anaesthetized and the doctor performs an artificial surgery such as an incision, but does not conduct any procedure (Rajagopal). The significance of using placebos lies in its ability to potentially improve the well being of patients. However, as easily as it can be an effective treatment in clinical treatment, it can also be an extremely immoral practice in research and trials.

Placebo treatments are as old as medicine itself, and are exceptionally effective in dealing with psychosomatic symptoms (Shorter). There is no trace of specific dates to when placebos were first practiced. However, it becomes increasingly evident of its effectiveness in treatment throughout history. John T G Nichols, who was once a professor at Harvard, wrote in 1893:

The average patient listens with much more interest to the prescription of his physician than to

his directions about hygiene. Expecting good results from the drug, he often imagines that he feels them. So great is the power of hope that, even in incurable diseases, a temporary improvement often follows each new prescription.

This influential statement displays the potential positive impact in medicine by easing patients' suffering through the implementing of placebo treatment. Although seemingly harmless as depicted in this quote, placebos come with a much more complex set of issues. The complexity of this topic is derived from peoples' moral and ethical codes. Despite ethical opinions varying case-to-case, clinical trials present a clear example of morally unjust behavior compared to the ethical and effective use as a treatment. To further investigate the ethics of these two usages of placebos, let us first analyze the use of placebos in clinical care.

The ethical debate surrounding clinical care is much less talked about in the medical field than that of clinical trials; there are many reasons why that is the case. By utilizing placebos in clinical care, doctors increase patients' happiness at a much higher rate than that of trials involving placebos. The benefits of placebo based treatment whether through surgery or pharmaceutical treatment are abundant and an extremely important part of modern medicine.

A recent study conducted by two Danish physicians, Hrobjartsson and Norup, shows the numbers of physicians that utilize treatment placebos. Out of 185 general practitioners, 86 percent reported they had used placebos interventions in the past year. Of those 86 percent, 48 percent reported using placebo treatment ten or more times. Tilburt and Colleagues conducted a similar study in the United States reporting out of 1300 physicians in rheumatology, 57 percent were said to have used placebo treatment effectively in the past year. Physicians were said to have generally reported positive results and attitudes towards their treatments (Colloca).

A major concern for most Doctors is whether they are deceiving their patients ethically. If the patient wants an effective treatment but instead receives a placebo, does that make the treatment unethical even if the treatment produced positive results? This question is what ethicists and doctors have been debating for over 30 years. Some scientists say that no matter what the treatment, the patients' right to have full informed consent is compromised therefore rendering all placebo

treatments unethical (Lichtenberg). But is that really the case? To better answer this question, let us look at two cases in which these concerns are addressed.

#### Case 1:

A 45-year-old man suffering for many years from diabetes and hypertension underwent a second leg amputation. Severe pain following the surgery was treated with injections of intramuscular pethidine, an opioid analgesic. His pain virtually unabated, the patient demanded additional therapy. The staff decided to administer, in addition to pethidine, intramuscular saline. They explained to the patient that injectable saline had been used as an effective painkiller, and that they anticipated that it would help his pain as well. The treatment produced an impressive analgesic effect, to everyone's satisfaction (Lichtenberg).

The issue of deceit is not a question in this case. This example is the purest way of benefitting the patient by improving his well being through a placebo injection. The moral issue of deception is not present in this case because the doctors clearly expressed to the patient what treatment he was receiving and the expected effects. The benefits here are greater than simply relieving the patient's pain. There is also the fact that the placebo may also produce less undesirable side effects than other potentially dangerous medications (Lichtenberg). Thus, leading to be a safer and potentially more affective method of treatment.

The issue of informed consent plays a large role in peoples' judgment of ethics in medicine. With informed consent jeopardized, people often are quick to call the action immoral and unethical. However, the notion that all placebos are unacceptable and immoral due to lack of informed consent is simply ignorant. "Disclosing to the patient that he is receiving a placebo does not necessarily diminish its effectiveness." Another argument against treatment placebos states that the successful placebos are more dangerous than failed ones because they perpetuate deceit by lying, or avoiding truthful answers to legitimate questions that patients might have regarding side effects, drug interactions or informed consent (Cahana). These critics pose an interesting question of what happens after the placebo has been issued, and what if something goes wrong. The answer is quite simple. If the patient demands to know the name of the pill or treatment, he shall be told. If he expresses

worrisome questions, or any questions at all, concerning the effects or how the pill works, he shall be told that as well. The patient can refuse any treatment he pleases (Lichtenberg). For one reason or another, people have this misconception that placebos are top-secret medical treatments that must never be released to the patient. That is simply not true; the patient has every right to intervene and ask what he is receiving.

Placebos in clinical care are not always a simple sugar pill or saline injection. That's the beauty of treating patients with placebos; there is a wide variety of safe alternatives to potentially harmful medications. To legitimize this idea let us look into a case containing an alternative placebo.

#### Case 2:

A 32-year-old mother of three is being treated for an agitated depression by means of hypnotherapy. In the course of one hypnosis session, the client envisions a bloody scene whose meaning is uncertain but which alarms her terribly. Refusing to continue with the therapy, she demands medication. The treating psychiatrist, seeing no alternative, prescribes imipramine at a starting dose of 25mg, explaining to the patient that effectiveness generally takes two to four weeks at a dose of 200-300mg. The day after taking her first 25mg dose, she reports that a remarkable improvement has taken place and virtually all symptoms have subsided. She continues, diffidently, her psychotherapy. Attempts to discontinue the medication meet with immediate failure. Explanations by the suspicious psychiatrist that the medication requires higher dosage and longer duration are shrugged off by the client (Lichtenberg).

To dissect this case let us analyze it in sections related to common controversy. First, informed consent is absolutely not an issue in this case. The doctor clearly gave the patient an informed briefing on the specific pharmaceutical name, effective dosage and time frame. Secondly, let us interpret the patient's well being as affected by the doctor. The patient presented clear issues that the psychiatrist observed and gave what he presumed was the best treatment for the well being of his patient. Another interesting point of this case is the method of placebo. The placebo is an active medication given in small dosages to act as an inactive placebo. This adds a whole dimension of placebo usage. A doctor can prescribe an active

substance at a low dose to treat patients in a more diverse approach. This clears up the issue of "deceit" completely, thus rendering placebo treatment completely ethical and potentially safer than active treatments.

So, with the basic understanding of placebo treatments and two cases presenting controversial issues we are now able to ask the question, when are placebos ethical to use and what constitutes ethical? The hardest part of utilizing placebos is knowing when it's appropriate. Luckily, doctors have guidelines put in place by the Declaration of Helsinki and the Federal Drug Administration. These guidelines serve to justify the use of placebos in situations that are deemed necessary. These guidelines include:

- The intentions of the physician must be benevolent: his only concern the wellbeing of the patient. No economical or emotional interest should interfere.
- The placebo, when offered, must be given in the spirit of assuaging the patients' suffering, and not merely mollifying him, or otherwise failing to address his distress.
- When proven ineffective the placebo should be immediately withdrawn. In these circumstances, not only is the placebo useless, but it also undermines the subsequent effectiveness of medication by undoing the patient's conditioned response and expectation of being helped.
- The placebo cannot be given in place of another medication that the physician reasonably expects to be more effective. Administration of placebo should be considered when a patient is refractory to a standard treatment, suffers from its side effects, or is in a situation where standard treatment doesn't exist.
- The physician should not hesitate to respond honestly when asked about the nature and the anticipated effects of the placebo treatment he is offering.
- If the placebo helps the patient, discontinuing the placebo, in absence of a more effective treatment, would be unethical (Clinical Ethics).

Placebo use in clinical practice is a very useful and extremely effective tool. There is no question that with misuse placebo treatment would be unethical. However, the goal of doctors' in their respective fields is to offer the most effective treatment to benefit the wellbeing of the patient. There are not always treatment for diseases and minor discomforts, those people who suffer chronically are able to be given a potentially life changing placebo treatment that improves their

quality of living; something most rational people would agree is the goal of medicine.

Changing gears, let us now compare the ethical and beneficial use of placebos in clinical care to the ethically questionable and immoral use in clinical trials. The comparison can be summed up in one quote from Alex Cahana and Simone Romagnoli's article in the *Journal of Anesthesia*. "Clinical trials are not designed to promote the patient's best interest; they are designed to answer valuable scientific questions." This quote can be interpreted a number of different ways, but in this context the authors are implying that the motives behind research placebos are strictly to discover new medical feats, rather than benefit the patient who is participating in the study.

Clinical trials are experiments in which the effectiveness of new pharmaceuticals and improvements on existing treatments are tested. The complexity here lies in the number of various fields in which placebos can be used. Before analyzing the ethics of clinical trials one must first be familiar with the terms used in the field. As previously referenced, the actual definition of placebo carries two definitions. In the case of clinical trials placebo can be defined as a false substance used in controlled experiments to test the efficacy of another drug.

Scientists use placebos in clinical trials for two reasons. First, producing a placebo effect to determine the clinical efficacy of a treatment, and second, as a control in an experimental situation (Chanah). To obtain results from a test the doctors must issue one test group a placebo; this is where the ethical debate begins.

The declaration of Helsinki provides the outline of the ethical debate concerning clinical trials. The declaration states, "every patient, including those of a control group, should be assured of the best current diagnostic and therapeutic method." The complication here is that doctors sometimes forgo an available treatment purely for the sake of the test results, thus rendering the patient that received the placebo uncured or left suffering minor to severe symptoms. The best example of this dilemma is introduced by Dr. Robert Temple of the U.S. Food and Drug Administration. During an interview with the *Dallas Morning News*, Dr. Temple gave an example of a trial that was conducted using a research placebo for a drug trial. The trial involved a group of test subjects given antihistamine to test the potency of a new drug to treat allergies. The other group was given an inactive medication. The control group suffered minor allergies. When asked about the trial Dr. Temple responded, "Its not unethical to do that trial. There's no conflict" (*Dallas Morning News*). However, there is a conflict of

interest, which is specifically stated in the Declaration of Helsinki.

The Declaration of Helsinki clearly provides the “clinical equilibrium” to doctors and patients; a method of ensuring that testing a new drug with placebo or no treatment at all when a known therapy exists is in fact contrary to the patients’ interests (Chahana). The Declaration of Helsinki was revised in 2001 stating that placebo use in trials was ethical when “minor conditions” or “scientific methodological reasons” dictate so (Cahana). Because of this revision scientists and doctors are much more lenient on what they consider to be a “necessary” use of a placebo as a control. The room for interpretation is far too large not to be taken advantage of; thus stirring the ethical debates that we see in today’s media.

The first ethical argument that weighs heavily on this issue is centered on patients not receiving adequate care due to receiving a placebo in a trial. The “best proven therapy” is a term that implies an already proven medical treatment available to patients. If an inactive placebo is used as a control in a trial where a proven therapy exists, the trial is unethical. “Ethically, the clinicians are always expected to provide their patients with the best choices of treatment other than placebo, and the best available treatment as a positive control other than placebos is preferable to the patients” (Zhang). Unfortunately, not all doctors follow these assumptions. There are many factors that play into the misuse of placebos in clinical trials. Most notably the influence of major drug corporations more concerned with innovation of new drugs to turn a multi-million dollar profit as opposed to giving patients an active and effective treatment as a control.

“The major difference between the clinical use of placebos and their employment in research is that doctors will prescribe a placebo in hope of actually benefitting the patient, whereas researchers use them in understanding that they will act as truly inactive comparators” (Zhang). The major downfall of placebos in clinical research is the problem presented in this quote. The ethics of intentionally not giving someone a treatment when a proven therapy exists is simply immoral.

Placebos in clinical trials are not necessarily always unethical. The exceptions to this rule would be when a treatment is truly nonexistent or undiscovered. Then and only then would a placebo pill or inactive medication be appropriate in a research setting. In all other cases, already proven or existing treatment must be used as a control in order to maintain the ethical justification of the experiment.

The ethical dilemma of research versus treatment placebos can be analyzed in a scholarly manner in order to determine the morality of each.

By using placebos in certain situations in clinical care, the doctor potentially benefits the patient in ways that he could not otherwise achieve without a placebo. Under the appropriate circumstances, doctors are able and in my opinion obligated to provide the best option for the patients’ well being through utilization of a placebo treatment. Although placebo testing in drug trials has led to remarkable discoveries in the pharmaceutical industry, it is not an appropriate method when a known treatment exists. Clinical treatment is an effective way to benefit the patients’ well being in an ethical and moral fashion.

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