

APS POSITION STATEMENT ON THE USE OF PLACEBOS IN PAIN MANAGEMENT

In the spring of 2003, the board of directors of the American Pain Society asked the APS Ethics Committee to formulate a position statement for the Society concerning the use of placebos in clinical practice (cf, reference 2). A subset of the Ethics Committee under my direction composed such a statement based on the available scientific and ethical literature. We then sought feedback from the entire ethics committee as well as numerous prominent voices in the literature and presented the statement to the membership for discussion at the 2004 annual APS meeting in Vancouver, British Columbia, at both a symposium and an ethics special interest group meeting. The resultant document was approved by the APS Board and is published here for widespread distribution to the membership.

— Gregory Terman for the APS Ethics Committee.

Summary

The American Pain Society (APS) opposes the inadequate treatment of pain using any therapeutic modality including the use of placebo. The placebo effect is ubiquitous in pain management, but the deceptive use of placebos and misinterpretation of the placebo response to discredit the patient's pain report are unethical. An analgesic effect from a placebo, moreover, does not provide any useful information about the genesis or severity of pain. The ethical use of placebos is justified only as a part of studies of therapeutic efficacy in consenting subjects and not as ongoing treatment. Informed consent is essential in all therapeutic situations, including the use of placebo.

Definition

Placebo is a treatment thought not to have a specific effect and is literally translated from Latin as "I will please." In clinical trials, the "placebo response" often encompasses all of the therapeutic effects that take place in the "nontreatment" arm of the study, likely stemming from routine nursing and medical care, anxiety reduction by diagnosis and treatment, the therapeutic relationship, and the expectation of relief.²⁵ In clinical practice, the placebo response is a component of any therapeutic intervention and should not be minimized.⁵ However, the intentional clinical use of placebo in assessing and treating pain often involves the use of inert substances (eg, injection of normal saline in a nerve block), subtherapeutic doses of active substances (eg, intravenous injection of 0.05 mg of morphine in an adult), or sham procedures (eg, transcutaneous electrical nerve

stimulation electrodes placed but no current applied) under the pretense of using specific therapies. This practice has been criticized on ethical grounds because of the deception of patients involved.^{2,7,8}

Background

Pain is recognized as being a subjective experience, and self-report is considered the most valid indicator of pain. When patients with pain seek care, they have a right to expect that their health care provider will be honest with them and provide therapy that is based on rational, scientifically validated evidence.²⁶ It is widely acknowledged that pain is frequently undertreated. Inappropriate use of placebos is one of many ways that pain might be undertreated.

Many of the reasons commonly offered for the use of placebo pain medication cannot be justified on either a clinical or an ethical basis. Some physicians administer placebos in an effort to determine whether a patient's condition is organic or functional. A positive response to placebo has been interpreted as evidence that a patient's pain is "psychogenic," and that their pain complaints are greatly exaggerated or due to "malingering." It is important to note, however, that even when there is objective evidence of tissue damage, including postoperatively, many patients with pain complaints report relief from placebos.^{11,23} Moreover, there is no evidence of certain patients being "placebo responders." The same individuals might exhibit a placebo response under some conditions but not under others. Advances in our understanding of the neuroanatomy,¹⁶ pharmacology,¹³ and physiology⁴ of the analgesic effects of placebo have demonstrated these effects to be examples of the activation of powerful natural pain-inhibitory mechanisms within the central nervous system including those mediated by endogenous opioids.¹³ Thus analgesic responses to placebo clearly should not be used to invalidate a patient's pain complaints.

Placebo pain medication has also been used to "please" a patient who demands an analgesic that has potentially harmful side effects when the physician does not believe that such medication is clinically indicated. However, there is evidence that placebos can also mimic active analgesic agents in their ability to produce side effects and even toxic reactions.³ A review of 109 phase I trials found that 19% of volunteers experienced adverse events in the placebo arm.²⁰ In addition, patients most likely to receive placebo treatments are those who are disliked or distrusted by their caregivers,⁹ suggesting that some placebos might be given as punishments.

Administering placebos surreptitiously or deceptively to patients does not contribute to, and more likely undermines, understanding of the patient's clinical problem and the patient/health care provider relationship. Some physicians have sought to justify the deceptive use

of placebos on the grounds of beneficence—that the end (patient welfare) justifies the means (patient deception). Indeed, there are a number of studies that demonstrate that expectation is important in placebo responses to pain therapy, and that such responses are reduced when subjects are told they are receiving a placebo.^{4,6,15,17} However, placebo responses can still be observed in patients informed that an inactive drug will be administered,^{12,14,18} and placebo responses are known to rely on multiple factors, including not only expectation but also conditioning, desire for relief, memory distortion, and suggestibility.^{4,6,17,19,24} No studies currently exist demonstrating that patient outcomes are improved by using placebos with or without patient informed consent. This undermines the contention that patients must not be told in advance about, and consent to, the use of placebo, and that this failure to inform is for their own good.

In light of the above, APS guidelines have for many years warned against the use of “placebos to assess the nature of pain,” as well as “the deceptive use of placebos and the misinterpretation of the placebo response to discredit the patient’s pain report.”¹ Because of substantial anecdotal evidence that the use of placebos in patient care without patient consent remains in common practice, the APS deems it necessary and appropriate to reiterate and reaffirm its earlier policy and to amplify the underlying clinical and ethical basis for it.

Ethical Tenets

Central ethical tenets in providing health care include truth telling, fidelity, trust, and respectful care. There is broad legal and bioethical consensus that patients must be informed and provide valid consent before medical treatments are administered. Patients are entitled to refuse any and all medical treatment if they possess adequate decision-making capacity to do so. Deception of patients about clinical treatments violates the right of patients to consent to or refuse treatment. In placebo-controlled clinical trials, patients consent to the possibility of receiving a placebo rather than the active, experimental treatment. It is generally accepted that the use of placebos in clinical trials is ethical when harm to patients from delayed treatment is limited, when the alternative active treatment is unproven, and when there is a substantial potential benefit to future patients in establishing efficacy and/or avoiding harmful side effects of a treatment. Even this is controversial since the Declaration of Helsinki by the World Health Organization in 2000, which raised concerns about denying patients enrolled in placebo-controlled trials the benefit of treatments already proven effective.²¹ All agree that at the completion of a trial, subjects should be fully informed about the nature of the treatment received and then be free to seek the treatment of their choice.

In contrast to clinical trials, placebos have historically

been used in clinical pain practice to (1) invalidate the patient’s pain complaint or (2) protect the patient from “harmful” treatments. The first is scientifically and ethically unacceptable. Placebo response does not prove that pain is not “real” or unworthy of any real treatment. The second rationale is more complicated. As mentioned, placebos can themselves cause harmful side effects and might delay specific treatments, thereby leading to disease or symptom escalation. On the other hand, trials of pain treatments, particularly before invasive or irreversible treatments, are common in clinical practice, and such practice might hold elements of a scientific clinical trial within it. To find the least invasive or damaging treatment, sometimes a placebo option might be included in the therapies tried. Responses to a placebo injection or temporary procedure, for example, might suggest that the risks inherent in a permanent procedure are not warranted at present. Trials involving alternation between active and placebo treatments in a single patient (known as “n-of-1 trials”) might provide clinically useful and scientifically valid information.^{10,22} Nonetheless, even such uses of placebo (to guide rather than to constitute therapy) ethically require patient consent. The patient should a priori be informed that one of the treatments (eg, blocks or injections) received will be a placebo (containing little or no active ingredients). If a treatment decision is made on the basis of a positive response to this placebo administration, the patient should be so informed and counseled as to why alternate therapy might be more beneficial at this time.

Recommendations

The deceptive use of placebos and the misinterpretation of the placebo response to discredit the patient’s pain report are unethical and should be avoided.¹

The ethical use of placebos is justified only as a part of studies of therapeutic efficacy in consenting subjects and not as the ongoing treatment when the trial is over.

Health care providers, when using placebos, have an ethical obligation to ensure that placebos are not used for the punishment, deception, or long-term undertreatment of patients with pain.

The use of informed consent is essential in all therapeutic situations, including those involving placebos.

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