# Placebo Pain Medication

## *Ethical and Practical Considerations*

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The placebo effect on pain is a complex phenomenon. The unconsented use of placebo pain medication, however, raises concerns given the risks both to patient trust and to the medical profession's reputation in condoning deception, the inherent distastefulness of deception, the misuse of placebos that occurs, and the fact that the information obtained is often of negligible value. The main justification given for using placebos is based on the assumption that they are effective and beneficial to patients. We argue that placebo pain medication should be prescribed to patients only with their informed consent in scientifically rigorous single-patient studies. The results of such trials would constitute a particularly useful way of resolving uncertainty in the treatment of patients whose pain is poorly controlled.

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The placebo effect is a complex phenomenon.[1] The placebo response is believed to be composed of several independent factors[2] involving such characteristics as expectancy,[3] suggestibility, perception of the competency and friendliness of the physician,[4] and hypnotic ability.[2] It appears, in fact, that the placebo response represents a multiplicity of responses, each acting with its own mechanisms and efficacy.[1]

In recent years, two major approaches in placebo-response research have emerged. The first addresses the use of placebos in randomized controlled trials (RCTs)[5]; the second involves the use of sociopsychological approaches to study the influence of expectancy or suggestibility in predicting a response to intervention.[3] While neither approach encompasses the entire issue, both contain elements that are useful. The former provides methodological and statistical approaches for measuring the magnitude of the placebo effect, while the latter allows us to conceptualize the effect, not as a "magical" event outside the boundaries of biomedical knowledge but rather as a particular form of social interaction.[6]

The therapeutic use of placebo pain medication may be defined as the use of an inert or subtherapeutic dosage of medication, deliberately or knowingly, for its nonspecific psychological or psychophysiological effect.[7-10] Although the prescription of placebo pain medication without the patient's knowledge occurs in medical practice, the ethical implications of this practice are frequently overlooked.[7] This article explores the implications of placebo pain medication administration for the physician-patient relationship and examines its scientific underpinning in clinical practice. Unless otherwise specified, the term *placebo* will be used to denote subtherapeutic treatment without the knowledge of the patient.

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### PLACEBO PAIN MEDICATION AND DECEPTION

A number of different rationales have been given to justify the use of placebo pain

medication. Placebos are believed by some physicians to be useful in distinguishing between organic and functional conditions; others use them either to prove to a patient that his or her condition is of psychological origin or to unmask a patient who is believed to be malingering or exaggerating symptoms. Finally, placebos may be given to appease a patient who insists on a potentially addictive or harmful treatment when the physician feels that no treatment is indicated.

Secrecy is felt to be a necessary component of placebo administration because success is assumed to depend on the patient's ignorance and suggestibility.[7] It is precisely this secrecy, combined with its implications of deception, that is at the root of most of the ethical controversy.

A number of arguments have been made against the use of placebos. In medicine, patients and their physicians are viewed as moral equals.[11] Deceptive practices would be inherently wrong because they undermine the moral nature of that physician-patient relationship.[9] There is a risk to patient care in that patients who ultimately discover that they have been deceived may irretrievably lose trust in their physician or in physicians in general.[7,12,13] Furthermore, since deceptive practices escape the normal restraints of accountability, there is a serious risk that resorting to placebos may lead to decreased physician vigilance and prevent the treatment of an underlying, undiagnosed problem.[13]

Other reservations have been expressed concerning placebos. The risk to the medical profession in condoning deception as a legitimate medical practice is damaging the honorable reputation of the profession.[7] A question has been raised whether it is ethical to charge the same for a sugar pill as one would charge for other pain medication.[14] Finally, the prescription of placebo pain medication could be seen as reinforcing an unhealthy attitude toward medication that has been encouraged by drug advertisers' suggestions of instant push-button alleviation of symptoms.[13]

In arguing for the use of placebos, the duty-based individual cannot deny the moral rule forbidding deception. One would have to therefore accept that either the deception rule does not apply when using placebos or some other moral rule mitigates it.[11] It has been argued that by not stating an overt lie as in the statement, "this medication may be of benefit to you," deception is not taking place[11,15] or that placebos are merely "white lies," which in this sense would mean that they are falsehoods not meant to injure anyone and have little moral import.[13] In defending the use of placebo pain medication from a consequentialist's perspective, it would be argued that the deception can be justified because it can result in a positive outcome. It is, in fact, this last justification that is most commonly used to support the use of placebos.

## AUTONOMY, BENEFICENCE, AND PATERNALISM

The prescription of placebo pain medication appears to be at variance with the usual approach taken with medical treatment decisions. It is standard medical practice to obtain informed consent before embarking on any treatment. Among the information that should be provided to the patient in this process is the nature of the proposed treatment, the benefits and risks of the proposed treatment, and the benefits and risks of the alternatives, which include the option of no treatment.[16,17] Although informed consent is usually viewed as a legal concept, it is essentially an ethical imperative designed to promote the values of personal well-being and self-determination.[18] The patient's right to determine his or her health care is widely recognized in current ethical theory.[17,19,20] It is our fundamental respect for individual choice that is expressed by the principle of autonomy.

The use of placebo pain medication clearly violates the principle of autonomy. Placebos began to be used at a time when the placebo effect was the most that physicians had to offer patients[21] and the guiding ethical principle was paternalism. Paternalism, however, fails to capture our fundamental respect for patients.[22] Today, physicians are involved in a cooperative effort with their patients that involves shared decision making.[18]

According to the principle of beneficence, physicians attempt to do "good" for their patients.[19,23] It is this principle that is used to justify using placebo pain medication. One argument supporting placebo pain medication would be as follows: The patient comes to the physician with the expectation that something will be done to alleviate the bothersome symptoms. Given the nature of this particular illness, a placebo would be as effective as any other medication. It would, therefore, be advantageous to prescribe the placebo, inasmuch as one would be minimizing the potential side effects and addictive potential of pain medications. In other words, the benefit to the patient is such that the principle of autonomy should be overridden. This argument assumes placebo pain medication is an effective intervention.

## PLACEBO PAIN MEDICATION

### Practical Considerations

The rationale for using placebo pain medication despite concerns about the practice of deceit and the overriding of patients' autonomy is the assumption that placebos are useful to patients. This further assumes that they have been given correctly and that the placebo response was understood by those giving it. These assumptions, however, are not supported by the literature. One survey of house officers and registered nurses in a university teaching hos-

pital revealed that patients receiving placebos tended to be those with whom the staff were having interpersonal difficulties and who were disliked or those who had failed to respond to standard treatments or both.[24] In that study, physicians interpreted a positive response to placebo intervention as evidence of a functional disorder even though the response to placebo does not equate with "nonorganicity" of a symptom.

Moertel et al,[25] however, found that very self-sufficient individuals with heavy responsibilities who were thrust into the unaccustomed dependency of a disabling illness were particularly vulnerable to the placebo effect. Goodwin and his coworkers[24] point out the irony that patients with multiple complaints and poor relationships with their physicians are, if anything, less likely to respond to placebos than are patients with good relationships with their physicians. The evidence of Goodwin et al suggests that placebos are more likely to be given to patients who, because of their presentation or personalities, are disliked by the treating team.

IN OUR HOSPITAL, the documented use of a placebo in pharmacy and nursing records has been a relatively infrequent occurrence. Our consultation service has been able to identify a number of factors for which placebos were prescribed: (1) patients had a history of pervasive interpersonal difficulties; (2) the medical history was often long and unusual; (3) medical interventions were often followed by a worsening of the condition with new complications; (4) the relationship between the health care team and the patient was poor; and (5) the prescribing physicians had a simplistic and inaccurate conception of the placebo effect, usually seeing administration of the placebo as a way to "fix the problem" (ie, the patient will stop complaining or the symptoms will be shown to be functional).

### Case Example

Ms A was a young woman with known inflammatory bowel disease and a history of long-standing family and characterological difficulties. She was a demanding and controlling individual who was difficult for the staff to work with. She complained frequently of her pain and demanded narcotics in a way the house staff believed was inappropriate. As a result they decided to give her a diluted dosage of narcotics without her knowledge to "see if the pain was genuine." This was done and the patient's complaints increased, and thus, the attempt was stopped. Relations between the patient, her family, and the treating staff deteriorated to the point that one of the interns was physically assaulted by the patient's father. Subsequently, after surgery for removal of a substantial portion of her small bowel, the patient signed herself out of the hospital against medical advice.

The use of a placebo in this case resulted in further deterioration of an already tenuous relationship. In using the placebo, a message was given that the patient's pain was spurious. The attempt to wean her from the narcotic did not consider the physiological aspects of narcotic dependency. Finally, an opportunity was lost. The very real personal and interpersonal difficulties of this patient were not dealt with. In summary, our experience seems to confirm the impression of Goodwin et al[24] that administration of placebo pain medication is more likely to be selectively used in patients who are unlikely to benefit from it and to be given by physicians whose rationale for their use is questionable.

## ALTERNATIVE APPROACH

### Informed N-of-1 RCT

In weighing the risk to patient trust and to the medical profession's reputation in condoning deception, the inherent distastefulness of deception, the misuse of placebos that occurs, the fact that the information obtained is often of negligible value (typically displaying a lack of understanding of the nature of the placebo effect), and the risk of decreased physician vigilance against the occasional benefits that may occur, we believe that placebo pain administration is difficult to justify. Brody[14] does not advocate an absolute moral prohibition against placebo use, but he does establish a prima facie presumption against it, placing the burden of proof back on the user.

Benson and Epstein[21] are of the view, however, that "the placebo effect demands greater comprehension and must be allowed to survive if medicine is to provide optimal care." A number of authors[8,11] have advocated obtaining informed consent before embarking on the therapeutic use of placebo medication. This approach has the advantage of eliminating the deception toward and lack of self-determination of the patient and although it could be argued that it undermines the efficacy of a placebo, this is not supported by the widely known fact that a placebo response is obtained in research studies where informed consent is given.

We go further than previous authors in advocating that the current methods for single-patient studies be extended to situations where placebo pain medication is given with a patient's consent. By comparing the response to a placebo with the response to a particular therapeutic agent in a rigorous manner, one should be able to determine whether the use of the agent has demonstrable clinical value. Clinical research trials commonly use placebos to establish the value of an active drug within a particular study population. With modifications, this procedure can be applied to the everyday clinical setting by using an N-of-1 RCT. The N-of-1 RCT is a refinement of clinical practice that can

be used to replace the traditional trial of therapy in any situation in which the benefits are not well established.[26] As outlined by Guyatt and coworkers,[26] the method involves the following series of steps:

1. In a situation in which the benefits of a particular treatment are not clear, the clinician and patient agree to test the efficacy of a particular medication or dosage in relieving pain.

2. The patient then undergoes a randomized sequence of pairs of treatment periods with the primary drug in question and the placebo. The order of the treatment periods is randomized so that each period has an equal chance of involving active drug or placebo.

3. As far as is possible, both the clinician and the patient are blind to the sequence of treatment periods. The length of the periods will be determined by the half-life of the active drug.

4. Using an agreed on set of criteria, both the physician and patient carefully monitor the treatment targets to document any possible differences between the treatment periods. Simple visual analog scales and questionnaires addressing key symptoms such as pain severity or duration, related symptoms, or pain-related disability can be used easily by the vast majority of patients and staff.[27]

5. The alternating treatment periods are repeated until a clear difference or clear lack of difference between the two periods emerges.

6. The code is broken and the results are discussed openly with the patient.

### Case Example

Ron was a 36-year-old former alcoholic who had problems of recurrent pancreatitis for more than 2 years. Despite having stopped drinking 2 years ago, he had episodes of acute chronic pancreatitis approximately every 6 weeks. These episodes led to hospitalizations, considerable acute pain that was mostly unresolved by medication, nasogastric tube suction for a week or two, poor nutrition, and the ever-present threat of surgery when he had a pseudocyst formation.

FOLLOWING one episode of acute pancreatitis, his morphine regimen could not be totally discontinued and it remained at a relatively high dose of 100 mg every 8 hours. All the physicians involved in the case believed this was necessary. His oral medication was carefully monitored and he seemed to be using the drug appropriately.

However, Ron began to visit other local emergency departments with increasing frequency, presenting with acute episodes of "pancreatitis." During these episodes he would ask for and often receive several doses of meperidine hydrochloride for pain control since his problem was well documented. However, supportive evidence for acute pancreatitis was minimal.

On a repeated visit to our emergency department he was admitted for further assessment. At this time he had little evidence of an acute physical problem. He had decided that morphine was ineffective and was receiving large doses of meperidine hydrochloride subcutaneously (150 mg every 3 hours) with little report of relief. He and his wife were having more marital difficulties and were receiving counseling. She was threatening to leave him. He was not drinking at the time.

In the hospital, he was quite demanding and angry that the nurses and physicians were not giving him enough meperidine to control his pain. He insisted that meperidine was the only thing that could control his pain and he resisted any attempts to try other medications or infusion techniques. One day a nurse found two used syringes in his bed after he was visited by a friend. He was confronted about this and stated that someone, "probably one of the nurses," put the syringes there. The team believed Ron was abusing meperidine and he was offered the option of an N-of-1 trial to prove his need for analgesics; he readily accepted.

The hospital pharmacist conducted the trial. All nurses and physicians were blinded to the medication. Syringes were prepared with either 150 mg of meperidine hydrochloride (a dose Ron found effective) or 10 mg of meperidine hydrochloride that was believed would be ineffective (placebo). He was given clonidine hydrochloride to reduce or eliminate any symptoms of opioid withdrawal. Then he was randomly given the contents of the syringes every 3 hours. His pain was monitored using a pain scale at the time of injection and 1 hour later.

The trial went on for about 5 days at which time Ron decided the trial should end. Analysis of the data showed that the placebo and the test dose were equally effective or ineffective at times with no consistency of pain response to either one. Ron was shown the results of the trial, seemed to accept them, and agreed to have the administration of his pain medication discontinued. Ron's visits for acute pain to hospital emergency departments stopped and his wife confirmed the impression that he was not taking any prescribed or illicit drugs.

The N-of-1 procedure requires a number of steps that include the following: (1) the clinician must decide that the procedure is indicated and that the information obtained will be useful in the treatment of that particular patient; (2) the patient must be willing to collaborate in designing and carrying out the N-of-1 RCT (without the consent of the patient, the trial cannot proceed); (3) the design of the study requires consideration as to the half-life of the medication, the frequency of the symptoms, and agreement on the clinically relevant targets; (4) the pharmaceutical services

will need to cooperate to set up the placebo design; and (5) some simple statistical analysis may be required.

Busy clinicians may either object to the additional work entailed or believe they lack sufficient expertise to carry out an N-of-1 RCT. Hospitals could address this problem by developing "pain services" or a pain committee, as we have done, that consists of a multidisciplinary team who would assist physicians in carrying out these trials while they are gaining specialized expertise in this area. Alternatively, pharmacologists could assist the clinicians. In addition, these specialists in pain management would make suggestions about current treatment and ensure that patients receive instructions in the various noninvasive techniques of pain self-control, which instruction then in turn leads to the patients' increased feelings of mastery and control. Making an illness more understandable and instilling a sense of caring and social support in patients has been shown to improve symptoms.[11]

N-of-1 trials can have an immediate effect on patient care. Sackett and coworkers[27] report that of 73 such trials attempted by their team, three could not be carried out, 13 were incomplete, seven were equivocal, and 50 yielded clear results. Of the 50 that showed clear answers, almost one half resulted in a change in treatment plan. Once these pain services are developed, both hospital-based and community-based physicians should be able to consult with them, particularly if they believe a trial of placebo pain medication is indicated.

## CONCLUSIONS

The rationale for using placebo pain medication, despite concerns about the practice of deceit and the overriding of patient autonomy, is the unvalidated assumption that placebo pain medication is useful to patients. This assumption is not supported by either empirical evidence in the literature or our clinical experience. We believe that placebo pain medication should be prescribed to patients only with their informed consent, in scientifically rigorous single-patient studies. Although we cannot understand why one would have to prescribe placebo pain medication without a patient's consent, we realize that such an entrenched practice will not readily disappear. It could be diminished, however, at the hospital level by developing expertise in pain control.

There are a number of advantages to using the N-of-1 RCT model when prescribing placebo pain medication with the patient's consent. The model establishes a collaborative and mutually respectful therapeutic relationship in which deceit plays no part. Furthermore, the results are scientifically more respectable and accurate, because they have been obtained using a double-blind design.

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