

The Current Status of Placebo in Hospital Practice

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Abstract: *Despite a voluminous literature on the topic of placebo, there has been little documentation of either actual clinical practice of prescribing placebo or the attitudes that surround it. Through a questionnaire survey of all head nurses of clinical units in one health services area of Connecticut, data were obtained on current practices regarding placebo use in the natural hospital setting. Multiple reasons for placebo use were given, and it was noted that patients receiving placebo tended to be viewed in certain ways. The effectiveness of placebo in symptom relief was reported as nearly double that reported in the experimental literature. Methodologic issues of the study and of placebo investigation, in general, are discussed. Because common clinical problems appear to generate most instances of placebo use, several issues pertinent to medical education are raised. Some future directions for placebo research are proposed.*

The history of medicine up until the present century is largely a history of placebo effects. Despite continued prescription of vile and bizarre substances, the physician continued to be a useful, respected, and honored member of society. Shapiro has summarized a vast amount of historical literature on the use and effects of placebo (1), defining placebo effect as the "psychological, physiological, and psychophysiological effect of any medication or procedure given with therapeutic intent, which is independent of or minimally related to the pharmacological effect of the medication or to the specific effects of the procedure, and which operates

through a psychological mechanism." The word "placebo" itself first appeared in the medical literature in the 1811 edition of Hooper's Medical Dictionary as an "epithet given to any medicine adopted more to please than to benefit the patient." "Placebo," translated from Latin, means "I shall please."

Little, if any, research before the 1950s was devoted to the placebo effect, but the past 30 years have seen the growth of literature in this area, with an increasing appreciation of the complexity of the phenomenon. Wolf in 1950 first described the end organ response to placebo (2), and there is increasing experimental evidence of the role of physiologic conditioning in placebo response "expectancy" (3, 4). Another area of research is the importance of the doctor-patient relationship (5, 6). Furthermore, there has been a growing appreciation that the placebo effect is influenced by the current state of the individual (7) as well as by social factors (8). Increased sophistication in clinical pharmacology since the introduction of the "blind test" by Gold (9) has helped researchers recognize that placebo cannot be considered "inert" by any means. Rather, placebo has been shown to have effectiveness in relieving a variety of symptoms. Reviewing 15 studies involving 1082 patients, Beecher estimated a placebo effectiveness of $35.2\% \pm 2.2\%$ in providing $\geq 50\%$ relief; placebo also has an array of side

effects, including nausea, dry mouth, headache, drowsiness, and rash (10). Dependence on placebo has been described (11).

Despite a voluminous literature on the topic of placebo, little documentation exists of the state of current placebo use and the prevailing attitudes that surround it. A review of placebo-related articles in the comprehensive *Iowa Drug Index* found no data on actual clinical placebo practices. It is also the authors' impression, derived from clinical contact through psychiatric consultation on medical patients, that most of the current knowledge of placebo is poorly appreciated. Placebo use is not uncommon and often seems to be symptomatic of some problem in the treatment situation.

The impetus for this study grew out of an effort to describe current practices regarding placebo use in the natural hospital setting. An initial attempt was made to study placebo practice using pharmacy records; however, because the most frequently used placebo, sterile saline, is not a formulary item, such standard centralized records were not available. The use of physicians as a primary data source was not considered feasible because of the large numbers of individuals involved. As a method of tapping pertinent data, the authors chose to survey head nurses who have information about large numbers of patients cared for by different physicians. Head nurses are also most directly involved in administering and monitoring medications, including placebo.

Methods

Questionnaires were sent to 150 head nurses at 11 medical hospitals. The floors surveyed comprised the total number of clinical treatment units in one health services district in Connecticut, including private and nonprivate services, acute and chronic care settings, house staff and attending staff, as well as all medical and surgical subspecialties. Two-page questionnaires, to be completed anonymously, covered a number of areas. Respondents were asked to identify (by multiple choices) the type of clinical unit they worked on and whether placebo was currently or recently in use. Those who responded "yes" to current use of placebo were asked to report on their most recent placebo case. A number of questions followed concerning patient personality, diagnostic and demographic characteristics, nursing care parameters, as well as reasons for and response to placebo use. Finally, several open-

ended questions were asked concerning attitudes and thoughts about placebos.

Results

Sample Characteristics

One hundred two of 150 questionnaires were returned and analyzed. Of the respondents, 49% (50/102) stated that placebo had never been used during their tenure as head nurse; 44% (45/102) were on units using placebo currently or within the previous 6 months. The ages of patients receiving placebo ranged from 9 to 90. There was no statistically significant distribution for placebo use by age or sex. A consistent trend was noted toward placebo use in facilities devoted to chronic care (9/9 questionnaires returned; 9/16 total), while the remainder of placebo use was evenly distributed through all types of units, as well as across socioeconomic classes.

Reported Indications for Placebo

Diagnostic categories of patients given placebo included a variety of medical-surgical conditions. When asked to list patient diagnosis or management issues indicative of placebo use, 91% of respondents listed pain (39 of the 43 patients). When asked to check off or list specific reasons for placebo use (see Table 1), in only three of the 39 patients with significant pain was treatment of pain listed as the sole reason for placebo use; all three of these patients made frequent demands for medication. Reasons for placebo use were often multiple. For eight patients (21%), one other reason was listed for placebo use in addition to the treatment of pain; two were given placebo because of suspected or known drug abuse; in three, placebo was used to treat anxiety (all three made frequent complaints for medication); two were given placebo because their symptoms were suspected not to be "organic"; and for one patient, placebo was used for fear of iatrogenic addiction. For 18 patients (46%), two reasons were listed for placebo use in addition to the treatment of pain: 9/18 were given placebo to treat anxiety along with a symptom considered not "organic." Of the remaining 14 patients (36%), eight had placebo to treat pain plus anxiety plus questioned organicity plus one other reason. The four patients for whom pain was not mentioned were on psychiatric units and were all given placebo for diagnostic purposes.

Table 1. Reasons for and frequency of placebo use

Reason for use	Percentage of patients ^a
Treatment of pain	91
Treatment of anxiety	51
Symptom suspected not to be "organic"	47
Patient a known or suspected drug abuser	33
Nothing else was helping	24
Diagnostic purposes	22
Fear of iatrogenic addiction	16
Concern for patient safety	7

^a Greater than 100% because multiple reasons for placebo use were given for all but three patients. There were no significant correlations among different reasons for placebo use.

Overall, placebo was used for diagnostic purposes in 10 patients (22%); when the symptom was considered not to be "organic" in 21 patients (47%); for known or questioned drug abuse in 15 (33%); when nothing else was helping in 11 (24%); and for concern for the patient's safety in three (7%). Twelve of 43 patients (28%) given placebo were known to the staff from previous admissions and had been given placebo previously.

Staff Perceptions

A number of questions addressed staff perceptions of the patients receiving placebo. Anxiety and emotional problems were seen as prominent in 86% (37/43). Twelve of 43 patients (28%) given placebo were considered less likeable than the average patient; 13/43 (30%) were considered more difficult than average to care for (six were considered both less likeable and more difficult); and 35/43 (81%) were considered questionable or not reliable. Eleven of the 12 patients listed as less likeable were also described as excessively anxious or emotional.

Placebo Response

Perceived response was assessed for both short- and long-term results. Placebo was seen as providing either some or marked positive initial response in 35/43 patients (81%) and as eventually effective in 68% of the cases.

Staff Attitudes

Data on nurses' attitudes toward placebo use were available for the entire respondent group of 102, regardless of whether placebo had been used on a

particular floor: 34% (33/102) believed that placebo is rarely indicated; 4% (4/102) believed that placebo use is never indicated; and none believed that it is often indicated. The conditions for which nurses believed placebo use to be acceptable included: when there is concern over drug abuse (24%); for diagnostic purposes (14%); for treatment (19%); for patient management (12%). Feelings (when described) that were associated with administering placebo were described by five (5%) as generally positive; by 34 (34%) as neutral and professional, as if administering any prescription; by 18 (18%) as somewhat negative; by 21 (21%) as negative or strongly negative. The suggestion for placebo use came from the nursing staff in 18/43 (42%) cases. Discussion with the primary physician took place in virtually all the cases.

Discussion

The results presented here raise several issues pertinent to the use of placebo in clinical practice. Certain limitations of these results should be noted. To begin with, the data emerge from retrospective reports. A "halo" effect may be involved in the reporting, especially in terms of nursing staff revealing information to a research group identified as academic and potentially critical. The "halo" effect might also operate as part of a cognitive dissonance phenomenon (12), which would make sense in terms of the prevalence of some of the negative attitudes toward placebo administration.

The study of placebo poses a number of methodologic problems. Placebo was seen in our sample as effective in both the short term 81% of the time and the long term 68% of the time, despite mixed attitudes toward its use. Further, placebo

was seen in chronic care settings as both indispensable and effective. In the experimental literature, placebo effects are noted to occur predictably at a rate of only approximately 35% (13). It has been pointed out (14) that placebo response is a complex phenomenon that is difficult to study in an experimental setting. The importance of the "reality" of the symptoms in question, the presence of stress, the degree of motivation, the credibility of the placebo prescriber, and the valence of the expectation to respond are all crucial variables that need to be elucidated. The placebo response may be more potent than the current experimental literature implies. Unlike laboratory studies, the patients given placebo in this sample were at least in part selected on the basis of interactional, behavioral characteristics.

This survey describes those patients most likely to receive placebo. Staff perceptions of anxiety or emotional problems in patients seem to be an important factor related to placebo use, as one or the other was present in 23/29 (59%) patients for whom placebo use was associated with pain management. Patients who present symptoms in an emotional or excessively anxious way are often considered unreliable. Only 4/23 (17%) patients viewed as excessively anxious or emotional were considered reliable. A physical cause for the symptom was questioned regularly if an "emotional" component was noted to accompany the pain. All but six of the 20 patients whose symptoms were suspected not to be "organic" were seen as excessively anxious or emotional. In our sample, the perception of unreliability increased in proportion to the presence of "emotional" problems in the patient, and the consideration of unreliability was tied to the use of placebo for diagnosis or treatment. This linkage of factors raises several clinical issues and areas for discussion.

It is important for the clinician to separate the style of illness behavior from the evaluation of the symptom in question. The clinician's evaluation of a symptom and eventual use of placebo seem to be strongly influenced by the patient's style of presentation. It is generally assumed, for example, that conversion reactions are more prevalent in "hysterical personalities," despite the evidence that this is not so (15, 16). It is our experience on the Psychiatric Consultation Liaison Service that anxiety and emotional factors are often either a personality response to illness (17) or secondary to an inadequately treated symptom. This observation is consistent with the Marks and Sacher study of the underuse of narcotic analgesics in treating pain in hospitalized

patients (18). The management of a complex symptom such as pain requires an appreciation of the interaction of biologic and psychosocial factors. Psychosocial factors often contribute to the phenomenon of pain and to illness behavior that may be seen as excessively emotional, anxious, or demanding. It is our inference, from questionnaire comments, that placebo use often results from the frustration of dealing with such patients. It is likely that a better appreciation and recognition of such factors would contribute to the resolution of clinical tensions. A vicious cycle frequently develops from this interaction (see Figure 1). The rational intervention usually involves a review of the medication strategy and an understanding of how the style of illness behavior often results in a treatment bias and contributes to a vicious cycle.

Other reasons for placebo use involve significant clinical misconceptions. Placebo is not a diagnostic tool. It is well established that placebo cannot be used to differentiate "organic" from "functional" disorders. Because of conditioning effects and other psychologic factors, placebo can relieve "organic" pain syndromes as well as other physical symptoms such as weakness, headache, and so on. The response of pain to placebo does not provide any diagnostic information.

The use of placebo to treat pain often results from the failure to appreciate that pain is a complex phenomenon with biologic, psychologic, and social subsystems components (19) which include the attitudes of the treater (20). The twin roots of the undertreatment of pain may be an inadequate appreciation of the pharmacology of analgesics and a sociocultural tradition that values stoicism (the sense that tolerating pain is desirable). Aside from inadequate or inappropriate medication scheduling, there is also a prevalent fear of iatrogenic addiction. In fact, when analgesics are properly prescribed, the rate of addiction is exceedingly low (21). The hesitancy to use analgesics in known or suspected drug abusers is a fertile field for growth of placebo use. Apart from the biased attitudes toward drug abuse (22) which make it a difficult treatment area, there is often a poor appreciation for certain clinical information that could make such situations more manageable. Such knowledge includes how to evaluate the presence of drug intoxication and withdrawal as well as a strategy to treat pain in an addicted patient (23).

Overall, several significant issues in placebo use are raised and future lines of study are indicated. Specifically, studies of placebo response must take

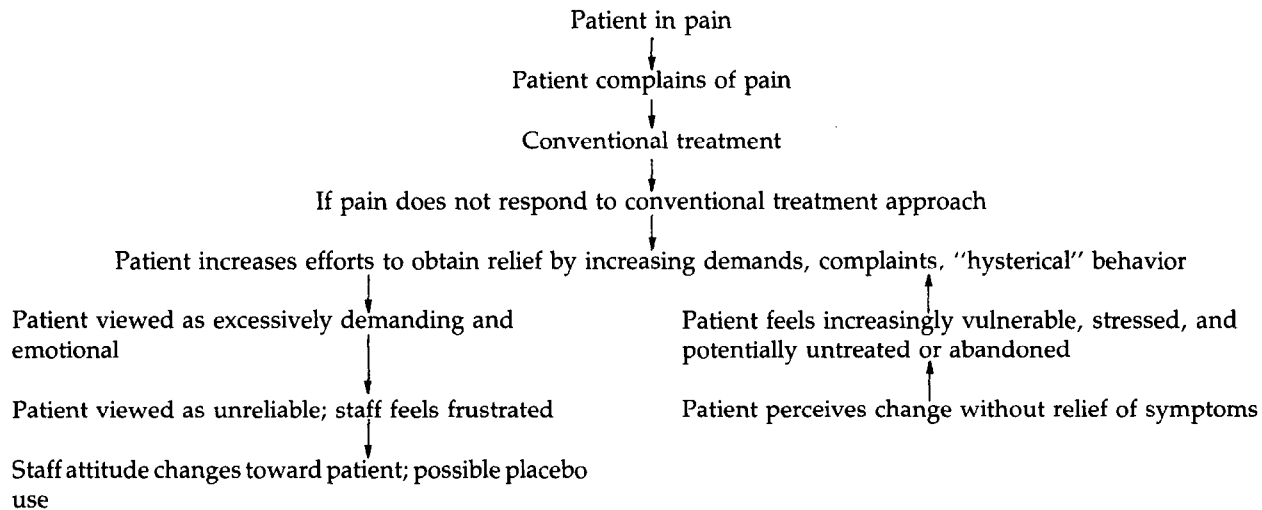


Figure 1. Example of how a vicious cycle can develop when the style of illness behavior is not separated from the evaluation of the symptom.

place in a naturalistic setting. Chronic care facilities may be an ideal place to do this because of the suggested frequency and stability of placebo use. Studies must coordinate social, psychologic, and neurophysiologic variables. For example, instruments that characterize social systems and other current methodology can be combined in a protocol to evaluate the effects of Naloxone on placebo response. Endorphins have been implicated in analgesic response (24) as well as in acupuncture response (25). If placebo response in pain involves conditioning of these central transmitters, it would be worth testing to what extent placebo-induced analgesia could be reversed by an opiate antagonist.

Finally, on the basis of our findings and experience, we are prompted to list current recommendations for placebo use. First of all, placebo is not a diagnostic tool. Whenever placebo use is considered, the clinician should ask himself "what characteristics of the treatment system have prompted the idea of placebo use?" Inadequate medication strategies, the style of illness presentation, and the nature of the patient-staff interaction all need to be examined. The study of placebo use thereby raises a number of medical training issues. Greater awareness of the vicissitudes of the doctor-patient relationship and the psychology of medicine giving and taking (26) need to be explicitly taught.

References

1. Shapiro AK: Contribution to a history of the placebo effect. *Behav Sci* 5:109-135, 1960
2. Wolf W: Effects of suggestion and conditioning on the action of chemical agents in human subjects—the pharmacology of placebos. *J Lab Clin Med* 29:100, 1950
3. Herrenstein RJ: Placebo effect on the rat. *Science* 138:677-678, 1962
4. Pihl RO, Altman J: An experimental analysis of the placebo effect. *J Clin Pharmacol*, March-April, pp. 91-95, 1971
5. Bogdanoff MD, Nichols CR, Klein RF, et al: The doctor-patient relationship. *JAMA* 192:45-48, 1965
6. Egbert LD, Battit GE, Welch CE, Bartlett MU: Reduction of post-op pain by encouragement and instruction of patients. A study of the doctor-patient relationship. *N Engl J Med* 270:825-827, 1964
7. Beecher HK: Evidence for increased effectiveness of placebos with increased stress. *Am J Physiol* 187:163-169, 1956
8. Pilowsky I, Manzop C, Bond MR: Pain and its management in clinical disease. *Psychosom Med* 31:400-404, 1969
9. Gold H: Cornell conference on therapy. *NY State J Med* 46:1718, 1946
10. Beecher HK: The powerful placebo. *JAMA* 159:1602-1606, 1955
11. Vinar O: Dependence on a placebo: A case report. *Br J Psychiatry* 115:1189-1190, 1969
12. Festinger L: *A Theory of Cognitive Dissonance*. Stanford, Calif., Stanford University Press, 1966
13. Sternbach RA: *Pain, a Psychophysiological Approach*. New York, Academic Press, 1968
14. Orne MT: On the social psychology of the psychological experiment: with particular reference to demand characteristics and their implications. *Am J Psychol* 17:776, 1962
15. Chodoff P, Lyons H: Hysteria, the hysterical personality, and "hysterical" conversion. *Am J Psychiatry* 114:734-740, 1958
16. Ziegler FJ, Imboden JB, Meyer E: Contemporary conversion reactions: A clinical study. *Am J Psychiatry* 116:901-909, 1960
17. Kahana RJ, Bibring GL: Personality types in medical management. In Zinberg N (ed). *Psychiatry and Med-*

- ical Practice in a General Hospital. New York, International Universities Press, 1964, pp. 108-123
18. Marks RM, Sachar EJ: Undertreatment of medical inpatients with narcotic analgesics. *Ann Int Med* 78:173-181, 1973
 19. Leigh H, Reiser M: *The Behavioral Foundations of Medical Practice*. New York, Plenum Press (in press)
 20. Hackett TP: Pain and prejudice. Why do we doubt that the patient is in pain. *Resident Staff Physician*, May 1972, 101-109
 21. Rayport M: Medical addiction to narcotics. *JAMA* 156:684-691, 1954
 22. Chappel JN: Attitudinal barriers to physician involvement with drug addiction. *JAMA* 224:1011-1013, 1973
 23. Giuffrida JG, Bazarri DV, Latteri FS: Surgery for drug abusers—anesthesia. *In* Bourne PG (ed). *A Treatment Manual for Acute Drug Abuse Emergencies*. Rockville, Md., Dept. H.E.W. Publication No. (ADM) 76-230, 1975
 24. Goldstein A: Opioid peptides (endorphins) in pituitary and brain. *Science* 193:1081-1086, 1976
 25. Mayer DJ: Opiate receptor mechanisms. *In* Snyder SH, Matthysse S (ed). *Neurosci Res Prog Bull* 13:94-99, 1975
 26. Byck R: The psychology of medicine giving and taking: A psychological basis for therapeutics. *In* Melmon KL and Morelli HF (eds). *Clinical Pharmacology*. New York, Macmillan, 1976

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