COMMENTARIES

Identified Placebo Treatment?

Donald F. Klein, M.D.

Brown (1994) suggests that identified placebo should be used as a treatment since many placebo-controlled trials show much improvement during placebo treatment. Among those improved during placebo treatment, we must distinguish those improved *from* the treatment from those who spontaneously remit. Studies of placebo response indicate that the most consistent robust predictor is episode duration. This argues against a specific placebo effect. Rather, benefit during placebo treatment is strongly related to the probability of spontaneous remission.

Brown argues that placebo treatment provides greater symptom relief than waiting list controls, but unfortunately waiting list controls are not "no treatment." For instance, Brown states that psychotherapy is more effective than waiting list controls but not more effective than pill placebo controls, whereas pill placebo is more effective than waiting lists. Anything worse than pill placebo is probably toxic.

Borgatta (1959) in a 1959 article suggests, on similar grounds, that we should use placebo psychotherapy. He specifically suggests waiting list limbotherapy. The correct treatment is to place the patient on a waiting list, then just prior to each appointment, call the patient and defer the appointment. When the patient stops calling back, he is cured. The issue of proper professional credentials for this clinical service was left unresolved.

Brown states that among depressed patients entering antidepressant clinical trials, few improved during the 1 to 2 weeks of single-blind run in treatment, but that during the two weeks of following double-blind treatment, placebo patients showed a sharp decrease in depressive symptoms. What are the data here? In any case, this does not provide evidence that placebo treatment gives greater symptom relief than no treatment. If anything, it indicates that receiving placebo is not of any marked initial consequence, but that it takes a certain period before placebo effects are manifested or spontaneous remission occurs.

One study compared placebo with no treatment in the context of the maintenance of gains. Rabkin et al. (1990) randomized depressive patients who had improved on placebo to either continue on placebo or to an informed discontinuation of placebo. The discontinuation was accomplished within the framework of affirming the patient's own ability to get better. Under these circumstances, follow up showed no difference in relapse rate. Although maintenance of benefit is not the same as initiation of benefit, there is no evidence in this context that the actual provision of placebo had any effect. Brown's argument that placebo treatment offers something over and above spontaneous remission or just a treatment setting needs better substantiation.

Brown points out that expectation is probably the best-studied component of placebo response and expectation of improvement is positively correlated with treatment outcome. Therefore, if people are given a placebo identified as an inert substance, will they have an expectation of improvement?

Brown's recommendation that identified placebo be used as treatment is premature. We have extremely little Phase II information concerning patients' reactions to identified placebo. The cited Park and Covi study must be substantially extended to allow for a better estimate of both the acceptability of identified placebo treatment and its putative efficacy.

If the promising results of Park and Covi are maintained, then randomized trials of follow up evaluation versus follow up evaluation plus identified placebo, are indicated. If these treatments are equivalent, one could

From the Department of Psychiatry, Columbia University, College of Physicians and Surgeons and the New York State Psychiatric Institute, Department of Therapeutics. Donald F. Klein, M.D.

Address correspondence to Donald F. Klein, M.D., Department of Psychiatry, Columbia University, 722 W. 168 Street, New York, NY 10032.

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not recommend the use of identified placebo. One would also be at a loss to know whether one should consider follow up and evaluation as a mode of treatment because of the lack of a no-treatment control. Is a no-treatment control, that is not a waiting list, feasible?

One possibility is to screen a group of likely depressives, such as high medical users, in a case finding, detailed, epidemiological survey. Those identified as having substantial but not suicidal depression could be randomly assigned to three classes. One class would receive no further contact until a final reevaluation. Another class would be offered placebo identified as a substance that has done many people good, and the third class would be offered placebo identified as an inert substance, but nonetheless, such inert substances are associated with benefit to many.

One wrinkle here would be the need for an estimate of the patient's belief whether they are actually getting placebo or not, as well as their view of the credibility of such treatment. Further, since it is likely that many patients would not accept going into a trial of identified placebo, the trial might be invalidated by a large differential refusal rate. This could, in part, be handled by the techniques developed by Rosenbaum and Rubin (1983) and Lavori and Keller (1988) for propensity score balancing.

Is there a down side to Brown's recommendation that identified placebo be initially prescribed? Brown estimates perhaps a 20% effectiveness rate. The most pessimistic assessments of specific benefit hover around 40%. Therefore, Brown suggests the use of a treatment substantially more ineffective than demonstrated specific treatment. Unless supported by a substantial body of controlled data, it would play into the hands of those who depict psychiatrists as artful, exploitative, manipulators who take advantage of the patient's gullibility. Further, if used for any large number of patients, one can be sure there will be both suicide attempts and completed suicides while on this treatment. Without an extensive body of data providing substantial efficacy for such a procedure, it is not clear if a defense of informed consent would hold.

The following scenario seems reasonable: First collect substantial Phase II data using the Park and Covi model. If this seems positive, follow with a trial of follow up evaluation plus identified placebo versus simple follow up evaluation. If that proves positive, then offering identified placebo in an informed way with a full discussion of alternative treatments might be an acceptable clinical procedure, but not till then. My guess is that if identified placebo is offered in the context of alternative superior treatments, it will not be widely accepted.

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