

## Some Ethical Concerns about Placebo Operations

### Placebo controls in surgical research can be performed ethically when certain criteria are met.

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Weijer C. I need a placebo like I need a hole in the head. *J Law Med Ethics*. 2002;30:69-72.  
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Miller FG. Sham surgery: an ethical analysis. *AJOB*. 2003;3:41-48.

There is a difference in kind and degree between a surgical and a pharmaceutical placebo. A sugar pill has no inherent risk, while a sham operation often does. There is, however, some agreement that placebo-controlled trials can be ethically acceptable in medical research. Usually this agreement depends upon the existence of clinical or procedural equipoise and an appropriate risk-benefit ratio. The degree of appropriate risk and whether this risk-benefit ratio pertains to the subject group collectively or to the individual research subjects are not settled issues, so it seems fair to ask what the appropriate criteria for placebo-controlled surgical trials might be.

Recently, fetal neuron transplant studies for patients with Parkinson's disease (PD) have stimulated the bioethical community's interest in the use of placebo control arms in surgery research. In these trials, the control group receives anesthesia, partial burr holes (not penetrating the skull), antibiotics, and immunosuppressive agents similar to those given to the treatment group, but without the transcranial needle injection of fetal neurons.

In discussing Peter Clark's [1] opinion of these trials, Charles Weijer points out that placebo operations as a control are not a requirement for scientifically acceptable research, even though a placebo control of some kind is sometimes needed [2]. Traditionally, placebos have been justified by comparison to everyday risk—if the placebo contains no greater risk than an individual encounters on an average day, then the placebo is acceptable. Obviously, all surgical placebos exceed this risk and fail to meet this standard. Weijer proposes that the risk-benefit ratio is an inappropriate comparison for nontherapeutic procedures because a direct benefit does not exist. Instead, he argues that risk should be counterbalanced by knowledge gained instead of benefit to the subject. For these fetal neural transplant trials, he argues that the potential for knowledge is too low compared to the risks involved for the placebo control to be ethically acceptable, and he also argues that patients not undergoing any sort of operation would serve as a more pragmatic control group.

Franklin Miller supports the structured use of placebo-controlled surgical trials [3]. He claims that when patients consent to research they are not owed the same duties by the research physician as by their treating physician (even when these are one and the same person). Miller distinguishes between the clinical obligations of beneficence and nonmaleficence, on the one hand, and, on the other, the obligation to minimize risks for research subjects—a standard accepted by many in the scientific community [4,5]. Weijer elsewhere indirectly challenges this risk-minimizing standard on legal and ethical grounds by emphasizing the continued clinical obligations of physician-scientists to their (and presumably other physicians') patients as research subjects [6,7].

Undoubtedly certain safeguards, such as using an objective third party to obtain consent from the patient/subject, may help subjects understand the different roles a physician-scientist plays.

Miller also claims that the ethical requirement that clinical research minimize risk is proportionate and not absolute. Accordingly, acceptable risk may exceed that of everyday activities, and the acceptability of this risk should be judged by the appropriate IRB. By highlighting a less risky intervention (arthroscopic knee incisions) [8], he suggests that placebo-controlled surgical trials with appropriate informed consent and a favorable research risk-benefit ratio are ethically acceptable and provide meaningful medical knowledge.

All surgical incisions have an intrinsic cost to the patient or subject, and the risk to both the treatment and control group subjects in surgical trials is such that the overall risk-benefit ratio may not favor one group over another; this is sometimes the case in pharmaceutical trials as well. Accordingly, a collective risk-benefit or risk-knowledge ratio that considers both the treatment and control groups together along with the clear and full disclosure of the consent form [3, 6] as it pertains to the risks and benefits for both the treatment and control groups should be considered when determining whether such a study is clinically and ethically acceptable.

When properly designed and implemented, randomized placebo-controlled surgical trials can yield important clinical or scientific knowledge in an ethically acceptable manner.

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## Questions for Discussion

1. Do you agree with Weijer that knowledge should be substituted for benefit in the risk-benefit ratio criterion for determining whether a surgical trial is ethically acceptable?
2. By arguing that the obligation to minimize risk is not absolute, does Miller give too much priority to patient autonomy in determining ethically acceptable research?

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