PEDIATRICS PERSPECTIVES

The Ethics of Open-Label Placebos in Pediatrics

Brit Trogen, MS, Arthur Caplan, PhD, Perri Klass, MD

Physicians have long debated the ethics of prescribing placebos as medical therapeutics.

Placebos (sham treatments such as sugar pills or saline injections) are thought to elicit improvements in clinical outcomes by mimicking medical therapies, thereby improving patients' expectations of getting better.[1] While the placebo effect plays a role in virtually every clinical intervention, the use of placebos as stand-alone treatments within medicine has largely been discouraged due to concerns about patient deception. Until recently, it was thought that for the placebo effect to emerge, the patient must be unaware they are receiving an inert substance. That physicians might mislead or deceive their patients, even for the sake of a clinical benefit, was generally viewed as morally unacceptable in the post–World War II era of informed consent and patient autonomy.

Over the past decade, however, concerns that placebos violate patient autonomy have been addressed by the development of "open-label placebos," treatments prescribed with full transparency and patient awareness. Patients offered an open-label placebo for the management of a given medical condition are informed that the substance is completely inert with no active drug component. Patients also are told, however, that such placebos have been found to produce benefits in individuals with their condition, preserving positive patient expectations. Because the open-label placebo method involves full disclosure to patients (and, in pediatric studies, to patients' parents), it is often referred to as "placebo without deception." Recent analyses have concluded that open-label placebos are generally consistent with the values of informed consent and patient autonomy.[2] Within pediatrics, the open-label placebo framework may represent a powerful new methodology with which to harness the placebo effect for clinical benefit in children's health.

The term "placebo effect" is often used colloquially to describe a small, confounding, or insignificant response. In both child and adult populations, however, placebos can reduce the frequency and severity of disease symptoms in patients at a level on par with many pharmacologically active drugs.[1] Several randomized controlled trials in adults support the effectiveness of open-label placebos in the treatment of a variety of conditions, including irritable bowel syndrome, migraine, and depression.[3,4] Although studies of open-label placebos in pediatrics

New York University School of Medicine, New York, New York

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Address correspondence to Brit Trogen, MS, New York University School of Medicine, 550 1st Ave, New York, NY 10016-1126. E-mail: brit.trogen@nyumc.org

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are scarce, reviews and meta-analyses generally find that children have higher placebo-response rates than adults, suggesting pediatric populations may benefit at least as much, and perhaps more, from attempts to implement placebo treatments into clinical practice.[1]

This is particularly compelling in light of the idea that open-label placebos could assist in reducing pediatric drug loads. Parents and physicians generally want to see children treated with the lowest effective doses of their medications. There also has been increased awareness in recent years of the risks involved in exposing children to medications that are prescribed "off-label," or that have never been specifically studied for long-term safety or efficacy in pediatric populations. Open-label placebos have been suggested as a safe and ethical way to replace, augment, or extend the effects of medications to reduce drug loads and medication side effects in children and adolescents.[5] A small study using open-label placebo for the treatment of pediatric attention-deficit/hyperactivity disorder (ADHD) found that ~40% of children could be maintained on half of their typical stimulant doses without any deterioration of symptoms as reported by parents and teachers.[5] Based on these considerations, the a priori prohibition of placebos from clinical practice may deprive patients of a potentially effective mode of treatment, while simultaneously exposing them to the heightened side effects, uncertain efficacy, and higher financial costs associated with pharmacologically active medications.

The few surveys available have generally found that parents and patients are open to the idea of using placebos therapeutically.[6] In the ADHD study described in the preceding paragraph, the authors found that parents expressed positive and supportive attitudes toward placebo treatments and that children believed the placebos were useful.[7] At the completion of the study, more than two-thirds of parents were interested in having their child take the placebo in the future, as they believed it would allow their children to take lower doses of medication and result in fewer medication side effects. Patients did not appear to view placebos as deceptive and, on the contrary, expressed significant interest and curiosity about the possibility of integrating placebos into their arsenal of treatments.[7]

However, there are some concerns over the potential negative effects of widespread use of clinical placebos. The precise functional mechanism of the placebo effect is poorly understood, raising concerns about the potential for unknown risks or "nocebo effects," whereby the expectation of an adverse effect by patients precipitates or exacerbates the experience of that symptom.

Perhaps more importantly, placebo use could potentially have a negative impact on broader patient and parental attitudes toward medicine and health care. It is possible, for example, that the widespread use of placebos would intensify the widely held expectation of "treatments" for every symptom, potentially exacerbating the problem of inappropriate overprescription of other medications.

More concerning is the possibility that placebo use could lead patients to develop false or misguided beliefs either about the placebo compound itself or the concept of "mind-body healing" overall. It is possible that patients and/or parents could equate the benefits they receive from placebos with a legitimization of other forms of so-called alternative medicines, or develop the inaccurate belief that "positive thinking" is sufficient to cure all manner of serious illnesses, forgoing proven treatments. Similarly, on learning of the benefits of placebos from their physician (or, just as likely, from the Internet or by word of mouth), individuals could feasibly attempt to "self-prescribe" inert substances to themselves or their children to lessen their use of other medications. Particularly in situations in which drug dosages must be maintained above critical levels over time, such as for antiseizure or hypothyroid medications, independent and unsupervised attempts to cut back or eliminate drug dosages could pose a serious health risk.

Finally, it is possible that the prescription of placebo treatments could damage trust in physicians, particularly if carelessly implemented. Although placebos have been suggested as possible treatment options for conditions that currently lack effective therapies, such as chronic abdominal pain, fibromyalgia, or psychosomatic complaints, offering what appears to be "fake drugs" for the treatment of these conditions could appear dismissive or delegitimizing of patients' suffering. Concerned parents may be even more offended on behalf of a suffering child. Because the psychological and medicolegal implications of providing inert substances for the treatment of real diseases have yet to be ascertained, it is difficult to predict whether offering placebo treatments may introduce added strain to the doctor-patient relationship in these cases.

These concerns must be carefully considered before the widespread professional endorsement and implementation of clinical placebos in pediatrics. As research continues to advance, however, the potential for open-label placebos to help reduce pediatric drug loads, particularly in conditions with strong psychosocial components like ADHD, abdominal pain, and migraine, should be considered. Forthright communication with families, as well as the development of careful guidelines and trials addressing which conditions may be most likely

to benefit from open-label placebo use, may help shape an appropriate clinical role. Although the practice must be closely monitored, the positive initial results from adult trials, along with evidence for heightened placebo responses in children and expressed patient and parental interest, suggest a possible limited role for open-label placebos in pediatric clinical practice.

ABBREVIATION

ADHD: attention-deficit/hyperactivity disorder

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