Nocebo Effect of Informed Consent in Interventional Procedures

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Placebo and nocebo effects have recently emerged as an interesting template to appreciate some of the intricate underpinnings of the mind-body interaction. A variety of psychological mechanisms, such as expectation, conditioning, anxiety modulation, and reward, have been identified, and a number of neurochemical networks have been characterized across different conditions.[1] The nocebo effect, the mirror phenomenon to the placebo effect, occurs when the expectation of a negative outcome precipitates the corresponding symptom or leads to its exacerbation.[2] Unlike the placebo effect, there has been much fewer studies on the nocebo effect. A PubMed keyword search on "placebo" returned 185,249 entries, whereas that of "nocebo" returned only 334 entries. This editorial aims at revealing the potential conflict between nocebo and informed consent in interventional pain management and discussing possible strategies to minimize potentially harmful nocebo effects.

HISTORICAL ASPECT OF INFORMED CONSENT

In ancient Greece, patient participation in medical decision making was considered undesirable. It was generally accepted that the physician's primary task was to inspire the confidence of the patient. Any disclosure of possible difficulties might, therefore, erode the patient's trust.[3] During medieval times, doctors were encouraged to use their conversations with patients as an opportunity to offer comfort and hope, while emphasizing the need for the doctor to be manipulative and deceitful. It was widely held that for the treatment to be effective the authority must be coupled with obedience.[4]

During the Era of Enlightenment, new views emerged such that patients had the capacity to listen to the doctor; however, it was still felt that deception was necessary to facilitate patient care.[3] During the 1800s the medical profession was split over whether to disclose a dire prognosis to a patient. However, most physicians of the time argued against informing patients of their condition.[4]

The doctrine of assault and battery has its roots in early English Common Law. Common Law is the combination of customs, traditions, and case law. This Doctrine forms the basis for the possible "injury" or "liability" incurred from surgery without proper consent.[3] As the concept of informed consent gained popularity during the 20th century, the courts extended the English Common Law Tort doctrine of negligence to the field of surgery by equating negligence with breach of duty and breach of duty with an incomplete patient consent. The failure of a physician to provide adequate information to the patient about his or her own treatment is interpreted by the courts as a breach of duty by the physician.[4]

MODERN FORM OF INFORMED CONSENT

During the last few decades, the way in which medicine is practiced has changed dramatically. The previous paternalistic approach, which emphasized beneficence to the exclusion of other principles, particularly autonomy, has been largely eroded. Unfortunately, however, physicians are not always able to determine their patients' best interests.[5] The case of Schoendorff v. Society of New York Hospital in 1914 has had the most impact on the doctrine of informed consent, in which the patient with a tumor underwent an operation to which he had not agreed.[3] In this case, Justice Benjamin Cardozo summarized "Every human being of adult years in sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patients consent commits a battery for which he is liable in damages."[3]

In recent years, along with the increasing popularity of shared decision making in health-care delivery, more patients have become interested in embracing their roles in making decisions regarding their own health.[6] Informed consent is the process by which a person authorizes medical treatment after discussing with clinicians the nature, indications, benefits, and risks of treatment.[6] Information to be discussed includes diagnosis, procedure, available alternatives, potential outcomes of each option, risks and benefits of each alternative, and the values of each potential outcome.

ORIGIN OF NOCEBO EFFECT

The nocebo effect was first named by Kennedy[7] as "Placebo reaction" in 1961, subsequently elaborated by Kissel and Barrucand.[8] The nocebo hypothesis proposes that expectations of sickness and the affective states associated with such expectations cause sickness in the expectant.[9] Two variants of these nocebo responses exist: one is characterized by new symptoms or a symptom aggravation associated with drug or placebo intake, although the chemical agent itself is not able to trigger these symptoms. Another variation of nocebo responses is the reduced efficacy of clinical interventions due to negative expectations or prior experiences.[10]

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Nocebo effects exist and operate during routine treatments, negatively affecting clinical outcomes. Nocebo effects are the direct result of the psychosocial context or therapeutic environment on a patient's mind, brain, and body, involving multiple factors, such as verbal suggestions and past experience.[11] Negative information and prior unsuccessful therapies may be particularly important in mediating undesirable outcomes to routine therapy. Therefore, consideration of nocebo effects in the context of patient-clinician communication and disclosure of interventional procedures may be valuable in both minimizing the nocebo component of a given therapy and improving procedural outcomes.

Nocebo effects can modulate the outcome of a given therapy in a negative way, as do placebo effects in a positive way. Importantly, these effects operate in the absence of a traditional placebo, forming part of everyday treatments.[11] To this extent, a balance must exist between communicating important clinical information and ensuring that every attempt is made to minimize negative instructions and a negative therapeutic context. This fine balance must take into consideration the patient's autonomy to make a decision based on all relevant information, with attempts to reframe how information may be delivered in a nondeceptive, yet reassuring way.[11]

PROPOSED MECHANISM OF NOCEBO EFFECT

The psychological mechanism of nocebo is thought to involve negative expectations and anxiety.[12,13] Although conditioning paradigms are more powerful in triggering placebo effects, both verbal suggestion and learning induce similar effects on nocebo development.[14] Cholecystokinin has also been shown to be involved in the hyperalgesic nocebo response.[15] Further, Scott et al[16] showed that, although placebo responses were associated with greater dopamine and opioid activity, nocebo responses were associated with deactivation of dopamine and opioid release, demonstrating involvement of the brain circuitry implicated in the reward response and motivated behavior.

Taken together, the underlying mechanisms of nocebo responses are much less well understood than those of placebo responses. In particular, the contribution of similar overlapping and distinct trajectories mediating nocebo versus placebo responses requires further investigation.[10]

CONFLICT OF CONCERN OF NOCEBO EFFECT AND INFORMED CONSENT

The principle of informed consent obligates physicians to explain possible side effects when prescribing medications or performing interventional procedures. This disclosure may itself induce adverse effects through expectancy mechanisms—that is, nocebo effects—contradicting the principle of nonmaleficence. Rigorous research suggests that providing patients with a detailed enumeration of every possible adverse event can actually increase side effects.[17]

One of the primary missions of physicians, dating back to Hippocrates, is the principle of nonmaleficence, Primum non nocere: "Above all do no harm." At the same time, the pinnacle of modern bioethics is informed consent, respect for person, and transparency.[17]

The relevant parallel dilemma is when the harmfulness of the nocebo effect may outweigh the good in proper disclosure of medical information to the patient, and where the duty to inform may therefore be suspended.[2] In view of the nocebo effect of informed consent, the harm in point does not exist; rather, the physician risks creating it by merely mentioning its potentiality. Moreover, this harm can be biologically real and cannot be dismissed as "merely psychological." This raises a different, new moral dilemma, which demands a search for a new moral balance between respect for autonomy and paternalistic nonmaleficence, and which ethicists are called upon to investigate.[2] This is of special importance with respect to the clinical practice of informed consent, where the very disclosure of potential side effects or complications can bring them about through a nocebo effect.

STRATEGIES TO MINIMIZE NOCEBO EFFECT

Wells and Kaptchuk[17] advocate that the perceived tension between balancing informed consent with nonmaleficence might be resolved by recognizing that adverse effects have no clear black or white "truth." They believe informing a patient about side effects is not a mere presentation of "facts" but is an important component of the art of medicine and requires the practitioner's clinical judgment. They have proposed a pragmatic approach for providers to minimize nocebo responses while still maintaining patient autonomy through "contextualized informed consent," an ethical procedure in which the disclosed information is tailored in a way that reduces expectancy-induced side effects while still respecting patient autonomy and truth-telling.[17]

These differences in reported adverse effects indicate that the way in which adverse events are presented affects not only risk perception but, more importantly, clinical outcomes. Rather than merely delivering detailed lists of specific adverse effects, clinicians should incorporate in their communication positive framing and percentage formats as opposed to negative framing and frequency format, thus possibly reducing nocebo effects by minimizing attention on the negative aspects of the treatment.[11]

Studies have shown that pain increases when harsher words are used to describe an upcoming experience. For example, 1 study showed that the use of the word "pain" resulted in patients reporting more pain than use of the phrase "cool sensation,"[18] whereas another study found that saying "you will feel a bee sting" before injection of a local anesthetic resulted in more pain than saying that the anesthetic will "numb the area [so that] you will be comfortable during the [following] procedure."[19] Pain interventionists may need to pay special attention to which words to choose when describing interventional pain procedures to patients in the process of obtaining consent approval as well during procedures. It may be a good idea to explain to the patients more about how the procedures will be done, the mechanism of the action of the selected procedures, and how successful they are in other people, and of course a confident, competent, and compassionate bedside manner will always help.

In summary, clinicians' efforts should be devoted to avoiding instilling negative expectations during the informed consent process, procedural information, and follow-up assessments so that the most effective patient-clinician communication can be pursued while unwarranted and untenable nocebo responses can be avoided.[11] In particular, description of procedures, a common interaction from doctors such as interventional pain practitioners, requires understanding of the potential of nocebo-mediated responses and their implications.

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