The Importance of Using Deferred Proxy Consent In Emergency Clinical Research

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Keywords: proxy consent, surrogate consent, research, clinical trials

INTRODUCTION

Obtaining informed consent from potential research subjects can be fraught with difficulty at the best of times. In emergency and critical care settings, informed consent from patients themselves is seldom obtained because they often lose decision-making capacity as a result of their severe illness. Although proxies are commonly recognized as the first party to represent an incapacitated patient in emergency situations, it is not always logistically possible to obtain their consent. Furthermore, time pressures and overwhelming emotions may decrease the value of surrogate consent in emergencies. To overcome these problems deferred proxy consent, or retrospective proxy consent, has been implemented as an alternative for informed proxy consent. Although there are inherent ethical challenges in applying deferred proxy consent, I will demonstrate that its application is crucial to protect patient populations in emergency clinical trials when following appropriate ethical guidelines.

ANALYSIS

Retrospective surrogate consent is applied when inclusion into emergency research involves randomization at the discretion of the investigator or the physician in charge. After inclusion of the patient into the study and after starting the study procedures, the proxy is informed, and subsequent consent for continuation in the study is requested. Research without informed patient or surrogate consent raises concerns about unethical practices and the loss of individual autonomy. The major objection to deferred informed consent, therefore, is that it erodes patient autonomy. According to bioethicists, retrospective proxy consent is ethically dubious when study procedures are finished before proxies can be informed and consent obtained. A patient may die, for example, after being enrolled in a clinical trial but before the surrogate can provide retrospective consent. Deferred proxy consent, therefore, most clearly violates principle 28 of the Declaration of Helsinki:

For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

Based on the premise that investigators need to seek informed consent from a surrogate but fail as a result of logistical impossibilities, some bioethicists conclude that the patient has been used as a

means to an end and that patient integrity is lost. Based on principle 28, these same bioethicists argue that retrospective proxy consent is unethical because informed proxy consent should be obtained before enrollment in clinical trials. Thus, they conclude that the principle of respect for persons is violated.

Although their ethical considerations are well intended, I believe bioethicists who subscribe to it use a too weak standard of autonomy and do not consider the patient's best interests. Under the best interests standard, a proxy must determine the highest likely net benefit among the available options. A patient's relevant autonomous preferences, however, often remain unknown to designated surrogates. If a patient's preferences are unknown, we should subscribe to the most suitable medical treatments that, on balance, provide greater probable benefits than harms for the patient. We should trust "physicians [to] use judgments about the ethical acceptability of research involving human subjects."

Physicians routinely make judgments based on the most suitable medical treatments on the balance of probable benefits and harms for patients. Furthermore, the Declaration of Helsinki makes it clear that one of the many duties of a physician is "to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research" (see principle 4 in World Medical Association, 2191). It is, therefore, justifiable for a physician to invoke soft paternalistic actions, such as enrolling a critical patient in a clinical trial. If deferred informed consent were found to be unethical, the inaction of a physician resulting from their inability to obtain informed proxy consent in an emergency situation would result in a far worse outcome–the death of the patient. Deferred proxy consent is also morally acceptable on the principles of justice and beneficence by providing a vulnerable patient access to novel treatments that may ultimately benefit their health and well-being.

As I have demonstrated, the principle of respect for persons is a primary concern in deferred proxy consent. It is important to recognize that autonomy of the patient is lost due to injury when a proxy is utilized; therefore, this can no longer be a guiding principle. However, the investigators should remind the surrogate that they should act as the patient, if competent, would have decided. By making decisions in this manner, the proxy ultimately respects the wishes of the patient to the best of their ability. It is also important to remember the elements of informed consent when implementing deferred proxy consent. Once the surrogate has been located by the investigator, they should be disclosed of the material information and recommendations of the plan. Afterwards, the investigator should perform a check to see if the surrogate understands these elements. The proxy should then be allowed to make an uncoerced decision and ultimately grant authorization of a chosen plan.

Looking at the lens of beneficence is complicated. Although there is hope that an individual patient will benefit, this is not more certain than the chance of non-benefit. Consequently, before an investigator decides to implement a clinical trial using an incapacitated patient, they must weigh risks and harm of the research subjects to the potential benefits of the trial to science and society. Conducting clinical trials in the context of an emergency or critical care situation may result in novel treatments that benefit vulnerable patient populations; therefore, if retrospective proxy consent is obtained, investigators should utilize the data appropriately. Clinical trials should only be implemented if they are projected to confer a potential benefit to the patient directly.

When considering nonmaleficence, investigators have a duty to relieve and prevent the suffering of patients, their relatives, and society. Confronting a bereaved surrogate after a patient has died following a clinical trial can add more harm to the situation. Clinical practitioners should aim to relieve undue burdens on all parties involved in the medical process. We should, therefore, adopt policies that prevent seeking deferred proxy consent after the death of the patient. If a surrogate withdraws

consent retrospectively, all collected trial data should be discarded. The purpose of such a rule allows the investigator to avoid introducing bias that could harm future patients. Moreover, we should act to expose subjects to minimal risks throughout the trial. We need to ensure patients are not being invited to undergo higher than minimal risks in the clinical trials without any chance for direct benefit. Holds should be placed on studies that confer greater than minimal risks to protect subjects from unnecessary harm.

Because we are considering persons in vulnerable states as a result of their emergency or critical care situation, the principle of justice is also relevant to this discussion. Frequently, vulnerable persons in emergencies are incapable of protecting their interests because of debilitation or cognitive impairment. Thus, the use of a proxy is paramount to providing consent to participate in clinical trials. We need to ensure that the trials and recovery do not place undue burdens on these populations. Additionally, we also need to ensure research is appropriately distributed equitably across patient populations. We should not withhold innovative therapies from these patient populations as opportunities to gain insight from these procedures is rare in emergency settings.

CONCLUSION

Although utilizing research subjects to conduct emergency clinical trials is challenging, this opinion piece has demonstrated that when we fulfil ethical conditions regarding deferred proxy consent, it is a viable option in clinical research. Physicians routinely make judgments based on the most suitable medical treatments on the balance of probable benefits and harms for patients. Having a physician decide to enroll a patient in a clinical trial through reliance on deferred proxy consent is a form of soft paternalism. Respect for patients is maintained so long as the investigator abides by the wishes of the surrogate once they retrospectively grant or withdraw consent to continue the trials. If a proxy decides to keep the patient enrolled in the study, new insights may be made regarding emergency medical treatments. It is imperative we strike a balance between risks and benefits among invested parties, so subjects are adequately protected in emergency clinical trials.

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