Sci Eng Ethics (2007) 13:289–295
DOI 10.1007/s11948-007-9025-6

ORIGINAL PAPER

Has Emergency Medicine Research Benefited Patients? An Ethical Question

Kenneth V. Iserson

Published online: 26 July 2007

Abstract From an ethical standpoint, the goal of clinical research is to benefit patients. While individual investigations may not yield results that directly improve patients' evaluation or treatment, the corpus of the research should lead in that direction. Without the goal of ultimate benefit to patients, such research fails as a moral enterprise. While this may seem obvious, the need to protect and benefit patients can get lost in the milieu of clinical research.

Many advances in emergency medicine have been based upon the results of research studies conducted both within the specialty and by others outside of the field. But has this research benefited patients? Has it followed the Hippocratic commitment "to do good or at least do no harm"? The answer is: yes, and no. This paper attempts to demonstrate this: first by citing advances from applied research that have benefited emergency department patients over the past three decades, and follows with some aspects of emergency medicine research that makes one question both its safety and its efficacy. While enormous gains have been made in patient care as a result of emergency medical research, ethical considerations complicate this rosy picture, and point to future areas of concern for researchers.

Some aspects of clinical research and research oversight fall short of meeting the ethical standards of safety and patient benefit. Research agendas are still driven largely by the availability of funds, both from private industry and from government agencies. Many vital patient groups are harmed by omitting or sorely under-representing them as research subjects, most notably those that are critically ill and injured. Finally, questions still arise about clinical researchers' fiduciary responsibility to their subject-patients. Even more important than the institutional safeguards, such as the Institutional Review Boards, is the individual researcher's moral compass, which must serve to protect the subject-patients of clinical research.

K. V. Iserson (✉)
Arizona Bioethics Program, The University of Arizona, 1501 N. Campbell Avenue, P. O. Box 245057, Tucson, AZ 85724, USA
e-mail: kvi@u.arizona.edu

Overall, emergency medicine research has been and continues to be a moral endeavor. Perhaps the greatest moral lapse has been the lack of attention to key populations within emergency medicine research, and the patients most needing acute intervention are the ones who suffer.

Keywords Emergency medicine · Medical ethics · Medical research · Clinical trials · Human experimentation

From an ethical standpoint, the goal of clinical research is to benefit patients. While individual investigations may not yield results that directly improve patients' evaluation or treatment, the corpus of the research should lead in that direction. Without the goal of ultimate benefit to patients, such research fails as a moral enterprise [1]. While this may seem obvious, the need to protect and benefit patients can get lost in the milieu of clinical research.

"Benefit" is defined as an improvement in the delivery of medicine. That is, research should demonstrate a way to decrease the delivery time, the cost, or the discomfort patients must face. Ideally, clinical research also should be undertaken with the aim of improving the diagnostic or treatment efficacy for a clinical condition.

Many advances in emergency medicine have been based upon the results of research studies conducted both within the specialty and by others outside of the field. But has this research benefited patients? Has it followed the Hippocratic commitment "to do good or at least do no harm"? [2] The answer is: yes, and no. I will attempt to demonstrate this: First by citing advances from applied research that have benefited emergency department (ED) patients over the past three decades, and follow with some aspects of emergency medicine research that makes one question both its safety and its efficacy. This paper argues that, while enormous gains have been made in patient care as a result of emergency medical research, ethical considerations complicate this rosy picture, and point to future areas of concern for researchers.

Yes, it has been Beneficial

Thirty years ago, at the dawn of emergency medicine as a specialty, clinical practice was largely governed by tradition. The first emergency medicine textbooks were published, and research within and applicable to the field was rudimentary [3]. Even the most up-to-date academic emergency physicians were hampered by an extremely limited pharmacopeia, by diagnostic and therapeutic equipment that had not changed for decades, and by hospital and prehospital systems designed for a bygone era of occasional ED use. Patients presenting to the ED suffered.

Since then, research in emergency medicine and the application of research from other fields has dramatically changed emergency medicine practice and markedly

improved ED patient outcomes. The following examples from the many diagnostic, therapeutic, and systems changes during the past few decades demonstrate the benefits from emergency medicine research.

Diagnostic Procedures

Diagnostic imaging has produced some of the most significant and beneficial changes for emergency medicine patients. Three decades ago, patients with head injuries received relatively useless skull radiographs or, if a more serious brain injury was suspected, either a time-consuming brain dye study or a diagnostic/therapeutic craniotomy. Today, head-injured patients receive a rapid and safe CT scan, which finds many more injuries and avoids unnecessary and dangerous surgeries. A similar situation existed with intra-abdominal pathology, including ectopic pregnancies. Where patients were once subjected to a peritoneal lavage, the barbaric culdocentesis, or a diagnostic laparotomy, today a rapid and painless CT scan, or even a bedside ED ultrasound, will often suffice [4–6].

The past 30 years also have led to many advances in laboratory testing that provide patients with more accurate diagnoses. The limited array of marginally effective diagnostic tests has become a wide variety of much more specific studies. For example, while the non-specific serum glutamic oxaloacetic transaminase (SGOT) and total creatine phosphokinase (CPK) were once used to help determine whether patients had had an acute myocardial infarction, troponins and other new bedside tests can now quickly "rule-in" many of these patients [7]. Thirty years ago, the use of D-dimers to test for pulmonary emboli, rapid Strep tests, bedside pregnancy tests, and rapid toxicological screens was only a dream.

Therapeutic Procedures

ED patients have also benefited from the many new pharmacological agents and the new uses for older agents that have been introduced over the past 30 years. Non-steroidal anti-inflammatory agents have provided a relatively safe and effective alternative to acetaminophen, indomethacin, and aspirin. Aspirin has come into its own as a valuable anti-platelet drug, especially for preventing and treating acute myocardial infarctions. Cardiac patients now avoid the complications from what was found to be unnecessary prophylactic lidocaine for myocardial infarctions, and from a number of safe and effective antiarrhythmic medications that more safely and quickly treat their cardiac abnormalities [8]. Arrhythmia treatment has also changed as a result of clinical research.

The variety of new, more effective, and less invasive/painful medications for patients with reactive and chronic lung diseases include the inhaled beta-agonists and steroids, replacing subcutaneous epinephrine, and the dangerous and less-effective intravenous aminophylline [9, 10]. ED patients in life-threatening hypertensive crisis were once treated with alpha methyldopa drips that often did not work, even after the 6 h it took to administer them [11]. What were once "sacred cows," some of the non-validated parts of medical practice, including the once-common psychiatric drug chlorpromazine; the horse serum-derived rabies

vaccine; digitalis for congestive heart failure; edrophonium and carotid massage for supraventricular tachycardia; and the opioid antidote that required reconstituting a pill, apomorphine; have been relegated to the back corner of medical history and replaced by safer and more effective agents.

Due to research findings, patients no longer are subjected to non-beneficial ED thoracotomies, or to the application of MAST pants that were ineffective in treating shock.

Systems/Prevention

Improvements stemming from research have also reduced the number of ED patients with preventable injuries. Innovative seatbelt design, airbags, safety glass in cars, and the use of better helmets in sporting, bicycle and motorcycle accidents have resulted in fewer and less severe injuries.

Those patients that do become seriously ill or injured often benefit from the research that led to establishing specialized centers to offer better care for some specific conditions. As a result, in many locales, patients with severe trauma, burns, or heart attacks, as well as pediatric patients, all receive first-rate treatment at these centers. Rape victims benefit from studies showing that the use of trained examiners diminishes their trauma while more proficiently gathering legal evidence.

Prehospital care has also advanced significantly, despite a paucity of good data to support its general efficacy. Thirty years ago, there were relatively few basic EMTs; today paramedics staff ambulances and helicopters in every large U.S. city [12]. Transport units have also changed, from the cramped quarters of modified hearses to units in which patient treatment can be delivered effectively. Most importantly, a uniform ambulance/fire/police dispatch system, known as 911, now encompasses most of the nation.

These represent only a few of the many advances that have completely changed the nature of emergency medical practice in a way that clearly benefits patients.

No, it has not been Beneficial

While clinical research has advanced patient care in emergency department and prehospital settings, the nature of the research, the researchers, and the application of results raise ethical issues concerning their beneficial nature.

Clinical Researchers

The first element in any research is the clinical researcher, often a physician whose patients may be the research subjects. Clinical researchers are fiduciary agents. That is, they must not put their own interests above those of their patients. Researchers must be careful in situations where their personal interests might conflict with those of patients or other researchers, and should not take advantage of their position. They must not only carefully guard their patient-research subjects' welfare, but also place those individuals' welfare ahead of their own interests. Is this being done?

Significance of Research

Every clinical study should be evaluated to determine what effect it will have on clinical emergency medicine practice, and whether those results are worth the risks to subjects. While all clinical research poses some risk, albeit often minimal, to the subjects, many results will lead to only incremental or insignificant changes in practice. Other studies fall into the "me too" category, simply repeating research (often with a less elegant design), and having little or no influence on medical practice. Ideally, Institutional Review Boards (IRBs) should monitor the significance of research at their institutions. This rarely occurs. Patient safety is another area that IRBs are supposed to monitor. The fact that so many clinical studies do not result in changes to clinical practice suggests that patient safety needs much more careful oversight.

Furthermore, as with all clinical research, the question of equipoise in emergency medicine studies should be addressed [13]. While all researchers should believe that the medication, technique, equipment, or system they are testing is at least no worse than what is currently used (equipoise), this situation rarely exists. If it did, clinical research would generate many more useful findings.

Other ethical concerns about the benefit of clinical research within emergency medicine—and, indeed, about all clinical research—are: Will significant results be adopted in a timely manner in the clinical setting? Will results be adopted into clinical practice despite adequate data? As in many other specialties, implementing even important research results is not immediate. Clinicians can be slow to adopt new drugs, systems, and equipment, despite their clear efficacy. When ineffective or potentially harmful changes are quickly adopted, such as with the administration of high-dose steroids for spinal injuries or the "black box" warning for the excellent, widely used (and inexpensive) drug droperidol, it is often because of misguided government mandates [14, 15].

Research Topics

Given the current climate of research funding, it is somewhat a matter of chance whether the research being conducted will have broad patient benefit. Research topics have as much to do with the money being thrown at certain clinical areas as with the effect any new information might have on patient care. Industry-sponsored studies of new drugs, of incrementally altered drugs, and to find new uses for older drugs flood the academic and non-academic research communities. A similar situation applies to the medical equipment/laboratory industry, as well as to government-sponsored research, which often is dictated by the agenda of the funding agency.

Research Subjects

The regulations governing research present many obstacles to recruiting minorities, children, pregnant women, those speaking other languages, and critically ill patients into research studies. The path of least resistance is to exclude them. This often

leads clinicians to extrapolate results to these groups, results that may not apply to them and that may, in fact, be harmful.

One group that should be included in emergency medicine research, but that has been routinely excluded due to impossible constraints on informed consent, has been critically ill, sometimes called "acute care" patients. These are patients who have suffered unexpected events carrying a high probability of mortality or serious morbidity *unless immediate medical intervention is provided*. [16] Due to their medical condition, such patients often have diminished mental status, precluding informed consent. Yet the needed immediate intervention is often the research focus. Such patients include those in cardiac arrest, those who have suffered a massive stroke, and those with severe injuries. In the United States, nebulous and difficult-to-institute federal rules guide this "non-consent" research [17]. Despite objections from some ill-informed academics, in mid-2007, the U.S. government finally initiated a series of non-consent studies of trauma treatments [18].

While performing non-consent research might appear to compromise patient safety, in fact the opposite is often true [19]. In the absence of acute care research on immediate interventions, unproven methods, tradition, and the results of small-animal studies often guide clinical practice. Clinical research results, such as those trials conducted with high-dose epinephrine, have stopped many unsafe practices. Safety and beneficence mandate that this type of non-consent research not only should continue, but actually should increase for critical emergency patients from whom consent cannot be obtained.

Conclusions

Much of medical care, including emergency medical care, relies on experience unsupported by investigation, so-called 'non-validated practice.' Over the past three decades, research done within the specialty and that done elsewhere but applied to emergency medical practice has improved the elegance of patient encounters, significantly benefiting ED patients.

Yet some aspects of clinical research and research oversight fall short of meeting the ethical standards of safety and patient benefit. Research agendas are still driven largely by the availability of funds, both from private industry and from government agencies. Many vital patient groups are harmed by omitting or sorely under-representing them as research subjects, most notably those that are critically ill and injured. Finally, questions still arise about clinical researchers' fiduciary responsibility to their subject-patients.

Even more important than the institutional safeguards, such as the IRBs, is the individual researcher's moral compass, which must serve to protect the subject-patients of clinical research.

Overall, emergency medicine research has been and continues to be a moral endeavor. Perhaps the greatest moral lapse has been the lack of attention to key populations within emergency medicine research, and the patients most needing acute intervention are the ones who suffer.

References

1. Spivey, W. H., Abramson, N. S., Iserson, K. V., et al. (1991). Informed consent for biomedical research in acute care medicine. *Annals of Emergency Medicine, 20*, 1251–1265.
2. Reiser, S. J., Dyck, A. J., & Curran, W. J. (Eds.) (1978). *Ethics in medicine: Selections from the hippocratic corpus* (p. 7). Cambridge, MA: MIT Press.
3. Wilkins, E. W. (Ed.) (1978). *MGH textbook of emergency medicine*. Baltimore: Williams & Wilkins.
4. Mueller, G. L., Burney, R. E., & Mackenzie, J. R. (1981). Sequential peritoneal lavage and early diagnosis of colon perforation. *Annals of Emergency Medicine, 10*, 131–134.
5. Moore, J. B., Moore, E. E., Markovchick, V., & Rosen, P. (1981). Peritoneal lavage in abdominal trauma: A prospective study comparing the peritoneal dialysis catheter with the intracatheter. *Annals of Emergency Medicine, 9*, 190–192.
6. Brenner, P. F., Roy, S., & Mishell, D. R. (1980). Ectopic pregnancy: A study of 300 consecutive surgically treated cases. *JAMA, 243*, 673–676.
7. Seager, S. B. (1980). Cardiac enzymes in the evaluation of chest pain. *Annals of Emergency Medicine, 9*, 346–349.
8. Brown, D. L., & Skiendzielewski, J. J. (1980). Lidocaine toxicity. *Annals of Emergency Medicine, 9*, 627–629.
9. Rothstein, R. J. (1980). Intravenous theophylline therapy in asthma: A clinical update. *Annals of Emergency Medicine, 9*, 327–330.
10. Gotz, V. P., Brandstetter, R. D., & Mar, D. D. (1981). Bronchodilatory effect of subcutaneous epinephrine in acute asthma. *Annals of Emergency Medicine, 10*, 518–520.
11. Barker, L. R., Slosberg, B., & Stine, R. J. (1980). Hypertension: Spectrum of problems and guidelines for management. *Annals of Emergency Medicine, 9*, 196–202.
12. American College of Emergency Physicians. (1980). Evaluation of an EMS algorithm system. *Annals of Emergency Medicine, 9*, 534–536.
13. Freedman, B. (1987). Equipoise and the ethics of clinical research. *The New England Journal of Medicine, 317*, 141–145.
14. Hurlbert, R. J. (2000). Methylprednisolone for acute spinal cord injury: An inappropriate standard of care. *Journal of Neurosurgery, 93*, 1–7.
15. Horowitz, B. Z., Bizovi, K., & Raymond Moreno, R. (2002). Droperidol—behind the black box warning. *Academic Emergency Medicine, 9*(6), 615–618.
16. Iserson, K. V., & Mahowald, M. B. (1992). Acute care research: Is it ethical? *Critical Care Medicine, 20*(7), 1032–1037.
17. Morris, M. C. (2005). An ethical analysis of exception from informed consent regulations. *Academic Emergency Medicine, 12*, 1113–1119.
18. Stein, R. (2007). Critical care without consent. *Washington Post, 27*, A01.
19. Iserson, K. V., & Lindsey, D. (1995). Research on critically ill and injured patients: Rules, reality, and ethics. *The Journal of Emergency Medicine, 13*, 563–567.