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A BRIEF HISTORY OF BIOMEDICAL RESEARCH ETHICS IN IRAN: CONFLICT OF PARADIGMS

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Abstract

During the past two decades, Iran has experienced a noteworthy growth in its biomedical research sector. At the same time, ethical concerns and debates resulting from this burgeoning enterprise has led to increasing attention paid to biomedical ethics. In Iran, Biomedical research ethics and research oversight passed through major periods during the past decades, separated by a paradigm shift. Period 1, starting from the early 1970s, is characterized by research paternalism and complete reliance on researchers as virtuous and caring physicians. This approach was in concordance with the paternalistic clinical practice of physicians outside of research settings during the same period. Period 2, starting from the late 1990s, was partly due to revealing of ethical flaws that occurred in biomedical research in Iran. The regulatory and funding bodies concluded that it was not sufficient to rely solely on the personal and professional virtues of researchers to safeguard human subjects' rights and welfare. The necessity for independent oversight, emphasized by international declarations, became obvious and undeniable. This paradigm shift led to the establishment of research ethics committees throughout the country, the establishment of academic research centers focusing on medical ethics (MEHR) and the compilation of the first set of national ethical guidelines on biomedical research—one of the first and most important projects conducted by and in the MEHR. Although not yet arrived, 'period 3' is on its way. It is predictable from the obvious trends toward performance of high-quality clinical research and the appearance of a highly educated new generation, especially among women.

Keywords

biomedical research ethics; history; Iran; paradigm shift; research oversight

INTRODUCTION

During the past two decades, Iran has experienced a noteworthy growth in its biomedical research sector. This growth has resulted in a prominent rise of Iranian scientists' share in scientific production in the world. At the same time, ethical concerns and debates resulting from this burgeoning enterprise has led to increasing attention to medical ethics, paid by faculty members and policy makers, which, in turn, has led to the establishment of several

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institutions, such as research ethics committees, research centers and departments of medical ethics, and to the production of guidelines and other materials on medical ethics. Several articles have described numerous aspects of this course of events in Iran. It can be claimed that Iran, as a developing country, has had its own unique model of scientific development along with establishment of ethical institutions and ethical oversight on biomedical research. After almost four decades since its very start, and more than two decades after its last major turning point, it seems to be the time to take a look at the course of development and evolution of the Iranian model of biomedical research ethics and research oversight as a noteworthy experience.

In their chapter in the *Oxford Textbook of Clinical Research Ethics* in 2008, Ezekiel J. Emanuel and Christine Grady described four paradigms of biomedical research ethics in a historical overview of the past 80 years of clinical research and research oversight, mostly in the United States of America.¹ In this article, I use their defined consecutive, but overlapping paradigms as a model to describe the main developments and events in the same field in Iran through the past decades.

THE FOUR-PARADIGM MODEL

According to Emanuel and Grady, the knowledge and practice of biomedical research ethics and ethics oversight have passed through four main periods in its historical course in the previous decades, since WWII. Each period is characterized by a paradigm.

The first period, beginning before World War II and lasting until the early 1970s, was characterized by ‘researcher paternalism’. In this period the underlying philosophy for research and research oversight was utilitarianism, which justified individual sacrifices for the social good. In this period, the highlighted ethical principle was social value and the key protection for research participants was researchers’ judgment, which was believed to be based on beneficence and professional integrity. The research participant was often considered ‘a passive subject of research’.

The second period, from the early 1970s until the late 1980s, was characterized by “‘regulatory protectionism’”. The triggering events for the paradigm shift from the first to the second period were revelations (including those stated in Beecher’s article) showing that even in research conducted by well-known researchers and in prestigious universities, sometimes, the basic rights of participants and the fundamental principles of biomedical ethics were violated. This suggested the necessity of adding external oversight and observance to the professional virtues of researchers for safeguarding human subjects’ rights. During this period, the key protection of research participants was from institutional review board (IRB) review and individual informed consent. The clinical trial participants were considered vulnerable and the underlying philosophy of biomedical research ethics was principlism whose highlighted ethical principle was independent review.

Triggered by the AIDS epidemic and the breast cancer movement, the third period began in the late 1980s and lasted until the mid1990s. This period is described as ‘participant access’. At the beginning of this period, the desperate need of patients (e.g. patients with HIV/AIDS or breast cancer) to access new investigational therapies transformed the concept of clinical

trial participants from ‘a vulnerable patient’ to ‘an informed consumer’. Subsequently, the key protection of human subjects changed to ‘respect for individual autonomy’ rather than independent review and supervision as it had been in the previous period. In this period, the underlying philosophy of research oversight was ‘individual rights-based theory’ and the highlighted ethical principle was informed consent.

The fourth period began from the mid-1990s. Triggered by genetic research among Ashkenazi Jews and aboriginal communities, and international HIV/AIDS research, put forth ‘host community collaboration’ as the key protection of research subjects, recognizing subjects as ‘active participants in the research enterprise’. Accordingly, the underlying philosophy of research oversight and the highlighted ethical principle transformed to communitarianism and ‘collaborative partnership’, respectively.²

It should be noticed that new values and protecting measures emerged in each new paradigm were added to –not substituted– the ones in the previous paradigm(s).

In this article, a historical review of biomedical research ethics and research oversight in Iran, I am going to show that this enterprise has passed the first period (although not completely) and is now going through the second period, and is expected to move towards the third and fourth periods in the predictable future.

METHOD

Sources of data and information in this historical study are as follow:

My personal experience: During the past eight years, I was in close contact with the developments in the field of biomedical research ethics in Iran. As the vice-president for research at the Medical Ethics and History of Medicine Research Center (MEHR) and department of medical ethics in the Tehran University of Medical Sciences (TUMS), as secretary of the specialized research ethics committee and member of the research ethics committee of TUMS, and from knowledge of other pioneer research institutes in Iran, I observed, first-hand, the development of this field in Iran. In addition, I was involved in compiling and updating the first set of national ethical guidelines for biomedical research in Iran. Teaching biomedical research ethics to graduate students, including PhD students, and organizing research ethics workshops for researchers and faculty members of universities throughout the country kept me apprised of the details and characteristics of this field in Iran.

Conversations with the main figures and scholars involved in biomedical research and research ethics all over the country—through meetings, conferences, workshops and other events—helped me to grasp a comprehensive picture of the past and present of biomedical research ethics in Iran.

Last, but not the least, a literature review of Persian and English resources helped to complete my view of this very subject. In the literature review, conducted mainly through August and September 2013, I used the key words ‘Iran’, ‘biomedical research’, ‘human subject’ and ‘ethics’ in various combinations to search the Web of Science and PubMed.

After finding relevant articles, I used the cited references to expand my review. I also reviewed relevant Persian literature collected over the years of my activity in this field; most available through the MEHR library.

BIOMEDICAL RESEARCH IN IRAN

Iran has a long historical tradition of academic medicine going back more than five thousand years. The first modern academic medical institute in Iran, however, was established in 1851, and the first modern university with a medical school, the University of Tehran, was founded in 1934.³ Biomedical research, however, blossomed decades later. As a matter of fact, the newly established medical schools in the 1920s, up until the early 1970s, were mainly focused on the immediate needs of the country to train practitioners and promote public health, e.g. vaccination and treating infectious diseases.

It was just in the early 1970s that new faculty members, mostly educated in western universities, started to launch the research enterprise in medical schools in Iran. In 1972, only a single Iranian article was indexed in Science Citation Index (SCI). This number increased to 610 in the next six years.⁴ In this period, most of the research was collaborative with developed countries like France and USA.

The first trend of rapid development of biomedical research, however, was halted by the occurrence of the Islamic revolution in 1978, and then by the Iraq-Iran war from 1980 to 1988. Lack of resources and skilled manpower due to the war and immigration of a large group of Iranian physicians and scientists, in addition to the immediate demands and burdens imposed by war to the health sector, were among the major causes of this pause. In the after-war era, a great deal of attention was paid to the research sector and after a short while the biomedical research enterprise began to recuperate. In the late 1990s spectacular strides were made in medical universities throughout the country, at least in quantity. The number of Iranian medical publications listed in the SCI Expanded database increased from 852 to 898 and then to 10,580 in 1978–82, 1993–7 and 2003–7, respectively.⁵ In 2009, Iran showed the fastest scientific growth in the world with a scientific output 11 times faster than the world average.⁶

Parallel to other kinds of studies, the number of clinical trials increased rapidly and special attention was paid to newly-emerging biomedical interventions and technologies, such as infertility treatment and in vitro fertilization (IVF), stem cell research, and organ transplantation. For example, in 2003 Iran became the tenth country in the world to produce, culture and freeze embryonic human stem cell lines.⁷

As a consequence of the growth of the biomedical research enterprise, significant ethical issues and concerns were raised and, subsequently, increasing attention was paid to the ethical and regulatory aspects of biomedical research.⁸ This attention was partly because of authentic ethical concerns and partly because of encountering the fact that international journals asked Iranian researchers who submitted their manuscripts to provide ethical approval from IRBs. Therefore, the need to develop institutions and instruments for biomedical research oversight was felt and the first steps were taken.

PERIOD 1: RESEARCH PATERNALISM

From the early 1970s, until the gradual development of research ethics committees in the late 1990s, this period was characterized by research paternalism and complete reliance on researchers as virtuous and caring physicians. This approach was in concordance with the paternalistic clinical practice of physicians outside of research settings during the same period. In fact, clinical research is mostly driven by physicians. Like other parts of the world, including USA, there was (and still, with some degrees of attrition, is) this assumption in Iran that physicians can be trusted to do what is best for their individual patients. Nobody saw any reason to change this assumption as a major protection, when it comes to clinical research settings.

Although the Declaration of Helsinki was known by Iranian researchers, implementation of its recommendations, including establishment of independent review boards, did not take place until the late 1990s. In fact, shortly after the first revision of the declaration (in which the necessity of independent oversight by institutional review boards was emphasized for the first time) was released (1975), the revolution (1978) and the war (1980) occurred in Iran, resulting in a temporary halting of biomedical research activities in the country. Even in the United States, the regulations governing IRBs did not come into effect until 1981. In Iran, however, it was two decades later that a blossoming research enterprise and the revealing of ethical shortcomings occurred, necessitating the establishment of oversight institutions.

PERIOD 2: REGULATORY PROTECTIONISM

In the United States, an article by Henry Beecher signaled a turning point which led to a paradigm shift.⁹ The revelations made by this article showed that violations of ethical norms in clinical trials had occurred, even in trials conducted in prestigious medical centers and by prominent researchers. Accordingly, it was agreed that the personal virtues of researchers could not be considered as the sole protector for subjects' rights and safety. In Iran, another later article played a similar role. In 1999, Arash Rashidian and Bagher Larijani published the results of their study on ethical assessment of clinical trials conducted in the TUMS from 1995 to 1998.¹⁰ TUMS is the oldest and biggest medical university, and the biggest funding body of medical research, in Iran; therefore, it can be considered an example of the best ongoing practices in the country.

The aforementioned article revealed that among 51 clinical trials reviewed in the study, only 1 (2%) mentioned 'ethical considerations' in the proposal or report; in only 6 (11.8%) of them, did research subjects know that they were participating in a research project; obtaining informed consent was mentioned in 4 (8%) of the reports (1 in the written and 3 in the oral form); placebo was used in 13 (32%) of the trials (in 10 of the trials subjects were imposed to some risks), while none of the participants had been informed about the possibility of receiving placebo; and in 41 (80.4%) of the trials, the costs of research-related interventions were paid by the research subjects (they thought that these were part of their treatment).¹¹ The findings of this study clearly showed the urgent need to adopting measures to prevent research misconduct in Iran, such as development of research-specific regulations and

bodies for research oversight. In the following years, these changes constituted a paradigm shift in biomedical research oversight in Iran.

Professor Bagher Larijani played a leading role in this paradigm shift. Given his strong religious and political background, Islamic and political authorities in Iran had a great deal of confidence in him; therefore, his activities in the field of medical ethics encountered no irresolvable resistance from them. This confidence was (and still is) an opportunity for the MEHR to introduce ethical discussions into the scientific and religious communities and show its necessity as a basis for policy-making regarding biomedical research issues.¹²

The main causes of such a paradigm shift in biomedical research oversight in Iran seem to be as follow:

1. After revealing ethical flaws occurring in biomedical research in Iran, the regulatory and funding bodies concluded that it is not sufficient to rely solely on personal and professional virtues of researchers to safeguard human subjects' rights and welfare. The very necessity of independent oversight, emphasized by international declarations, became obvious and undeniable. Also, the need for a set of concrete ethical guidelines for researchers was realized.
2. Advances and improvements in the field of research ethics in developed countries, along with developing international instruments (e.g. Declaration of Helsinki), had their own influences in Iran. Leaders in the field of biomedical research, and policy makers, as mentioned above, did their best to import and implement new measures of biomedical research ethics into the research enterprise of Iran. They realized that scientific progress in the country requires developing updated ethical infrastructures.
3. Pressure from editors of international journals, requiring Iranian authors to submit ethical committee permission, was another major drive behind this movement towards establishing research ethics committees in the country.

The main events of this period were as follow:

1. Establishment of the National Research Ethics Committee in 1999, and successively, formation of research ethics committees (RECs) in major medical universities and research institutes in Tehran and in other cities within the country.¹³
2. Compilation of the strategic plan for medical ethics in Iran through two intensive workshops.¹⁴
3. Establishment of an academic research center focusing on medical ethics (MEHR) in 2004 was a great leap forward in this field. Soon after its formation, this center began to organize and conduct research ethics workshops for researchers in the medical universities of Tehran and in other cities across Iran. In addition, this center funded and conducted several research projects in the field of biomedical ethics.

4. Compilation of the first set of National Ethical Guidelines on Biomedical Research was one of the first and most important projects conducted by and in the MEHR. Among their numerous directions and suggestions, these guidelines mandate obtaining informed consent from all research participants and set criteria for its validity in different settings and situations in accordance with international standards.

All the above mentioned changes and developments which characterize the succession from the first to the second paradigm in Iran, encountered some major criticisms and resistances within and outside of the field of biomedical research in Iran. Accordingly, it is difficult to say that the second paradigm is completely implemented. Rather, one can see a situation which can be named “conflict of paradigms.” The main elements of this conflict are:

1. Dominance of paternalistic approach to clinical practice, at least among a part of clinicians, even in academic centers in Iran. It seems ironic to expect a clinician to follow a different set of values when she is performing research than when she is practicing clinical medicine. For example, when the usual informed consent for a huge surgery is just one or two pages and the patient often do not have enough time to read it before signing, it seems ironic to ask the doctor to obtain an standard informed consent -containing several pages of information and a sophisticated process of disclosure and ensuring the voluntariness- when she wants to take 10cc blood from the same patient for research. In fact, the clinical medicine in Iran has taken some major steps towards an autonomy-based doctor-patient relationship during the past decades and – especially in academic settings- it cannot be considered completely paternalistic. Even some national projects have been conducted aimed to compile more autonomy-based informed consent forms for different clinical procedures. But the paternalistic approach is still forceful with major impacts on the field of clinical research.
2. Iranian national guidelines for biomedical research have been criticized to be inspired from the western guidelines. Sometimes they have been even accused to be nothing more than translated copies of western declarations and guidelines. Although the norms and instructions of Iranian national guidelines are about 80–90% similar to their western and international counterparts, it does not mean that they are just copies. In fact, a sophisticated process of cultural adjustment has been conducted for each of these guidelines and a large group of high-ranked religious and jurisprudential scholars, in addition to well-known researchers and philosophers and lawyers and ethicists have been involved in compiling these instruments. The existing similarity can be attributed to the similarity of the practical implications of different normative sources rather than copying or repetition.
3. Although the national guidelines for biomedical research are in accordance with the second paradigm of research oversight, some of rules which are ratified by the Islamic parliament are compatible with the paternalistic approach to clinical practice, which can be considered another source of the remaining conflict of paradigms in the field of biomedical research in Iran.

IS A “PERIOD 3” ON ITS WAY?

During the past several years, political sanctions imposed a negative burden onto the young research enterprise of Iran. But, regardless of short-term turbulences, it seems that this field has found its own way toward improvement and excellence in the foreseeable future.

Although not yet arrived, ‘periods 3 and 4’ are on their way. It is predictable from the obvious trends towards (1) performing high-quality clinical research and (2) appearance of a highly-educated new generation with a weighty proportion of academic degree holders, especially among women.

Advanced clinical research and innovations in Iran, like stem cell research, can provide promising treatments in the context of research. Therefore, securing fair participant access may become more important in the research enterprise and research oversight in Iran in the near future which will push them towards a paradigm shift to the 3rd period.

In addition, having a highly educated new generation, Iran has a great potential for more engagement of the public sector in debates and discussions on ethical and regulatory aspects of biomedical research, which is the main characteristic of the 4th paradigm.

CONCLUSIONS

In 1967, Marshal W. Nirenberg, American noble prize laureate, wrote an editorial column in Science about advancements in the field of biochemical genetics. He indicated: “Decisions concerning the application of this knowledge must ultimately be made by society and only an informed society can make such decisions wisely.”

As described above, having an educated new generation and advanced research enterprise, Iran has almost all prerequisites for moving towards the 3rd and 4th paradigms of biomedical research oversight. Learning from the experiences of developed countries, like the USA, in this field, may help Iranian researchers and policy-makers to go towards the 3rd and 4th paradigms without having the unwanted experiences which led to these paradigm shifts in the developed countries.

The four-paradigm model presented by Emanuel and Grady can be used as a basis for describing the historical events and developments of the field of biomedical research ethics and research oversight, as I used in this article for sketching such history in Iran. Because of close relations and exchanges among research institutes throughout the world, and the noticeable influences of changes and advances in developed countries on the developing world, it seems that such a model can be useful for describing past events and predicting future progress of this enterprise in other parts of the world.

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Biography

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