ORIGINAL RESEARCH PAPER

Volume-6 | Issue-12 | December-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 93.98

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

WHY ETHICAL SAFEGUARDS MATTER IN MEDICAL NANOTECHNOLOGY: PROSPECTS AND PROBLEMS IN THE DELIVERY OF NANOMEDICINE VIA MICROSURGICAL INTERVENTIONS

Medical Science

Tista Bagchi Professor University of Delhi, North Campus Delhi – 110007, India

ABSTRACT

Nanomedicine and medical nanotechnology are considered to constitute new frontiers of medicine on a number of counts. As with any such new scientific developments, significant moral and prudential concerns, which together come under ethical concerns overall, inevitably arise as regards the regulation of the implementation and use of these developments. The resultant need for ethical safeguards and regulations in nanomedicine gets compounded with the need for safeguards in microsurgical interventions given the prospect of combining the latter with, e.g., polymeric micelle-borne drug delivery. The modes of addressing the need for combined ethical safeguards and regulations adopted here are those of reasoning from common morality relating to bioethics and of initiating reflective equilibrium, with consideration of the respective prospects and problems of nanomedicine (including nanotechnological implementation) and microsurgery as known to date, with examination of certain key transnational guidelines in medical ethics, but focusing on this particular combination of the two.

KEYWORDS

Microsurgery; Nanomedicine; Medical technology; Bioethics; Ethical safeguards

1. Introduction: Why ethical safeguards?

Nanomedicine and medical nanotechnology, as relatively new branches of medicine and medical technology to emerge in recent times (Caster, Patel, Zhang & Wang 2017), are subject to ethical and regulatory principles and policy like any other branch of medical science, implementation, and technology. They are, in fact, subject to what one might call the Hippocratic covenant, which forms the basis of the Hippocratic oath that all professional ("mainstream') medical practitioners are required to take worldwide at the beginning of their careers. The following excerpt is of interest to the theme of this paper:

"I will follow that system of regimen which, according to my ability and judgement, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous." (Translation by Francis Adams, 1849, quoted by *Encyclopædia Britannica*, 2017)

It is desirable, if not essential, in fact, to understand the historical context of this excerpt in order to relate it to contemporary concerns in medical ethics and regulatory policy, keeping the ultimate professed goals of medical practice and research in view. The most comprehensive compilation of the corpus of Hippocrates' writings to date is Craik (2015).

Coming down to more contemporary concerns regarding the ethics and regulation of medical interventions for human patients or subjects, newer branches of medical research require a special kind of attention in regard to ethical concerns surrounding them. These concerns as relating to the particular domain of nanomedicine have been articulated with a good deal of clarity by Resnik & Tinkle (2007), who state that, among other things, "researchers, consumer advocates, and politicians have urged government agencies and private companies to proactively address the ethical, social and regulatory aspects of nanotechnology" (345). In this paper, an attempt is made to examine these concerns in regard to the combining of microsurgery with theranostic nanomedical technology.

2. Methods to arrive at ethical safeguards for new medical science and technologies

2.1 Moral rules: Gert (1998)

One method to be considered for application to ethics for new medical science and technologies is that of working out ethical safeguards for these in terms of absolute moral rules, such as proposed by the late ethicist / bioethicist Bernard Gert (1998) – of which the following six might be of interest in our context:

- "Do not kill"
- "Do not cause pain"
- "Do not disable"
- "Do not deprive of freedom"
- "Do not deceive"
- "Be fair"

Gert recognizes that, in actual cases to which these rules might have to be applied, it may be necessary to override one or more of these rules. For instance, with special reference to the medical domain, in providing particular medical therapies, it may be necessary to inflict some pain, at least for a period of time, in order to effectively deliver those therapies at targeted sites, and to ensure sustained treatment under appropriate hygiene, it is often necessary to temporarily confine a patient under hospitalization. A more dedicated approach to the issue of moral rules in the domain of bioethics, including biomedical ethics, is discussed in the following subsection.

2.2 A more comprehensive approach to medical ethics: Gert, Culver, and Clouser (2006)

A more dedicated text in the domain of biomedical ethics is Gert, Culver, and Clouser (2006). Therein they argue for *common morality* as the foundation for dealing with moral problems that arise in the practice of medicine. As they say in the Preface, they "provide a systematic account of our common morality as a public system", and thus they "do not merely accept our thoughtful moral decisions and judgments, but show that all of these judgments about cases and policies are related to and justified by this common moral system" (p. v). This common morality also encompasses rules of the sort outlined by Gert as mentioned in Section 2.1, above.

Comprehensive as this approach is, however, there is a problem with the application of this notion of common morality towards the development of ethical, including policy-oriented, safeguards in a millenarian (in the sense of future-oriented) subarea of medical research and extension such as nanomedicine, and this problem carries over into the possibilities of combining microsurgery with nanomedicine. This approach will likely become more favourably applicable once these medical methods come to be in widespread practice applied to human patients, but that is as yet to happen, ironically because there is already (and justifiedly) a strong regime of regulation and control in place in the matter of human-subject applications of these methods. Accordingly, in the subsection below, yet another, perspectivally different, approach to the development of ethical safeguards as applicable to the medical methods under consideration is introduced and considered. This is known as the method of Reflective Equilibrium.

2.3 Reflective Equilibrium

The term *reflective equilibrium* was initially applied to the principles of *logical reasoning* by the philosopher of mind and of science Nelson Goodman. The political and legal philosopher John Rawls then applied and popularized it as a method in the domains of ethics and the law (Rawls 1971/1999).

Reflective equilibrium is described as
(a) "the end-point of a deliberative process in which we reflect on and revise our beliefs about an area of inquiry, moral or non-moral", and
(b) it "consists in working back and forth among our considered

judgments" … "about particular instances or cases, the principles or rules that we believe govern them, and the theoretical considerations that we believe bear on accepting these considered judgments, principles, or rules, revising any of these elements necessary in order to achieve an acceptable coherence among them"(Daniels 2003/2016).

2.4 Application of the methods to medical praxis, science, and technology

Given this, the identification of principles and rules of morality that we take to govern the pursuit and praxis of medical science becomes imperative. This is where the groundwork laid out by Hippocratus becomes significant, and principles of justice in Rawlsian mode demand to be fine-tuned to respond to the domain of medical science.

Unfortunately, not everyone has considered judgments, especially in matters of ethics. There are all manner of social and cultural mores prevalent worldwide, some of which may entail conflicting ethical judgments across socio-cultural strata and subdomains, and hence entirely conflicting ethical outcomes might ensue from these. Large masses of people worldwide are often to be found in states of such basic deprivation that they may (although not necessarily or inevitably) be incapable of such introspection about their considered judgments, particularly in relation to medical crises or critical safeguards in healthcare and medical research. In addition, there are now increasingly documented instances of high-functioning professionals in domains such as medicine and surgery who are neurocognitively so configured as to be incapable of making or gauging the import of considered judgements of any ethical import: many of these individuals are "Cluster B" personalities who are found to have significant neurological differences from control individuals, which have been found to correlate with distinctive allelic characteristics (Jacob et al., 2005). Thus, the method of reflective equilibrium cannot be invoked as a default method in all possible situations that might arise in the pursuit of medical science and research or in the practice and implementation of medical methods. The only possible scenario in which it becomes feasible to use reflective equilibrium as an appropriate method to adjudge ethical implications is under the consideration of a group consisting of people who can and do have considered moral judgements that are relevant to the particulars of each case as well as experts in medical science and research who can provide the necessary technical information and insight relating to the particular case(s).

3. Microsurgical intervention and delivery of nanomedicine

3.1 Procedural issues

Combining (i) drug delivery via nanotechnology with (ii) microsurgical procedures such as fine incisions or laparoscopic microsurgery looks promising for a variety of medical problems, from malignant tumors to cardiovascular blockages to even fertility and assisted reproductive treatments. However, there has to be careful co-ordination between procedures belonging to the two different levels of magnitude, given that microsurgical procedures are performed at dimensions of <1 mm down to the level of multiples of micrometres (μm), whereas nanomedicine and more specifically drug delivery elements such as liposomes and polymeric micelles operate at dimensions of around 10-100 nanometres (nm).

Nanosurgery itself, of course, has long since been attempted using (a) atomic force microscopy with a nanoneedle, and (b) femtosecond laser surgery (as reported by Ebbesen & Jensen 2006); however, in this instance there is still considerable expense involved, as compared to the *relative* economy in employing microsurgery and nanomedical drug-delivery technology in combination, especially in a variety of medical-institutional situations globally. Also, given that nanosurgery is conducted at the level of the "really tiny", its scaleability for really meaningful surgical intervention is still in doubt.

For the two levels of magnitude, an analogy is to be found from different levels of organization found in (spoken) language. Language happens to be a multi-tiered organisational system, with details of the organisation at each "tier" or level of analysis being different (to some extent only) from one natural language (such as English, French, Hindi, or Japanese) to another. Out of these, there are two clearly noticeable levels, of two different orders of magnitude. Greatly simplified, these are (Akmajian, Demers, Farmer, and Harnish 2006):

(I) the *phonetic* level of speech-sounds (with their distinctive articulatory and acoustic features),
(ii) the *morphological* level of the building blocks of words (which encode both word-meanings and grammar).

3.2 Ethical issues: prudential versus moral

Besides what is morally right or wrong to do, ethical deliberation also encompasses what is prudentially correct to pursue – i.e., is likely to lead to desirable consequences in practical terms (a distinction made by Immanuel Kant, 1785/2002).

A "precautionary principle" has been proposed – however, "the principle can be scientific provided that (1) the threats addressed by the principle are plausible threats, and (2) the precautionary measures adopted are reasonable." (Resnik 2003: 329)

More generally: "As the science and technology of nanomedicine speed ahead, ethics, policy and the law are struggling to keep up. It is important to proactively address the ethical, social and regulatory aspects of nanomedicine in order to minimize its adverse impacts on the environment and public health and also to avoid a public backlash."

(Resnik & Tinkle 2007: 345)

Given these formulations already made in regard to nanomedical ethics, these merit further scrutiny in relation to the method of Reflective Equilibrium. The precautionary principle is of a piece with the principles that frame the method in question. This is to be subjected to both procedural and ethical scrutiny, needless to say, in keeping with the method concerned. It becomes especially vital to create and implement anticipatory safeguards under the precautionary principle given the "butterfly effect" power of microsurgical-nanomedical interventions to precipitate either positive macro-outcomes or cascaded damage that cannot be controlled or even remedied "down the line" after such interventions.

4. Existing regulation and safeguards

Some of the best guidelines for nanomedicine are those put out by the European Medicines Agency ("EuroMed") – including

- the development of block-copolymer-micelle medicinal products
- Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices
- committees to oversee specific domains, e.g.

(a) the Committee for Medicinal Products for Human Use
(b) the Pharmacovigilance Risk Assessment Committee
(c) the Committee for Advanced Therapies
(d) the Pediatric Committee.

In India, there are beginnings in the governance of nanomedicine and medical nanotechnology under the overall guidelines of the Indian Council for Medical Research (ICMR) and also the Department of Science & Technology (DST) – Bhatia & Chugh (2016).

Ethical concerns regarding the unbridled practice of nanotechnology, especially in the biomedical domain, are also expressed in the final chapter of Sundara Rajan (2016). These are primarily wider concerns regarding the misuse of nanotechnology in general, rather than being focused on nanomedicine and related micro- and nano-level technologies such as are under consideration here.

5. Conclusion: Towards a viable framework for ethical safeguards

To conclude, this paper has highlighted the positive prospects of combining microsurgery as a means of fine-tuning and further enabling nanodrug delivery in targeted ways, and at the same time, the need for ethical safeguards to regulate this combination. It has considered two prominent approaches for the determination of such safeguards, i.e., the common morality approach and the method of reflective equilibrium, and has suggested that the second of these approaches might be the more appropriate one in the current forward-looking scenario in nanomedicine and its technological dimensions. It has then gone on to examine ethical as well as procedural issues arising from the application of the approach to the combination of microsurgery and nanodrug delivery.

A point that needs to be further emphasized, in conclusion, is the following:

Ethical safeguards are not meant to unduly or unfairly constrain treatment and/or research in nanomedicine but are in fact meant to help patients and professionals/researchers navigate their way through the complex routes of new medical protocols and technologies. While there are of course safeguards that apply to microsurgery, and – increasingly – safeguards dedicated to nanomedicine in various parts of the world, the time has come to seriously consider and work out in detail ethical safeguards that are dedicated to the interface between the two.

This is with a view toward positive growth of further applications and developments in the combination of the two for better and better treatment options in nanomedicine and medical nanotechnological methods with a view toward benefitting people worldwide.

ACKNOWLEDGEMENTS

The author wishes to thank several members of the audience at the Thirteenth International Conference on Nanomedicine and Pharmaceutical Nanotechnology (NanoMed 2017) held in Rome, Italy, during July 24-25, 2017, for their responses to my presentation of this paper. An earlier professional development grant received from the National Institute of Science Technology and Development Studies, Council for Scientific and Industrial Research, India, helped to fund the research that contributed significantly toward this paper. Special thanks are due to A. J. Mixson of the University of Maryland School of Medicine for his thoughtful comments and for valuable discussion on related matters, and to Katharina Fromm, Sabrina Gioria, Ruba Ismail, and Silvia Mellace for their interest and support.

REFERENCES

1. Akmajian, Adrian, Richard A. Demers, Ann K. Farmer, and Robert M. Harnish (2010). Linguistics: An Introduction to Language and Communication, 6th edition. Cambridge MA: MIT Press.
2. Bagchi, Tista. 2012. Ethical principles behind policy on reproductive technologies in India. Paper presented at the Group Meeting of the Society for Indian Philosophy and Religion, American Philosophical Association Pacific Division Meeting, Seattle WA, April 3-7, 2012.
3. Bagchi, Tista. 2015. Between life-creation and policy formulation. In Science, Technology, and Development in India: Encountering Values, ed. Rajeswari S. Raina, 188-203. New Delhi: Orient BlackSwan.
4. Benatar, Solomon, and Peter A. Singer. 2010. Responsibilities in international research: A new look revisited. Editorial, Journal of Medical Ethics 36: 194-197.
5. Bhatia, Pooja, and Archana Chugh. 2016. A multilevel governance framework for regulation of nanomedicine in India. Nanotechnology Reviews, doi:10.1515/ntrev-2016-0083 (retrieved 7/16/2017)
6. Buchanan, Allen, Dan W. Brock, Norman Daniels, and Daniel Wikler. 2001. From Chance to Choice: Genetics and Justice. Cambridge: Cambridge University Press.
7. Caster, Joseph M., Artish N. Patel, Tian Zhang, and Andrew Wang. 2017. Investigational nanomedicines in 2016: A review of nanotherapeutics currently undergoing clinical trials. WIREs Nanomedicine and Nanobiotechnology 9(1) [January/February 2017], e1416

a. http://onlinelibrary.wiley.com/doi/10.1002/wnan.1416/full (retrieved 6/15/2017).

8. Craik, Elizabeth M., ed. 2015. The 'Hippocratic' Corpus: Content and Context. London: Routledge.
9. Daniels, Norman. 2003, revised 2016. Reflective equilibrium. Stanford Encyclopedia of Philosophy (Winter 2016 edition), ed. Edward N. Zalta, URL https://plato.stanford.edu/archives/win2016/entries/reflective-equilibrium/

a. (retrieved 7/14/2017)

10. Ebbesen, Mette, and Thomas G. Jensen. 2006. Nanomedicine: Techniques, potentials, and ethical implications. Journal of Biomedicine and Biotechnology 2006: 1-11. DOI 10.1155/JBB/2006/51516
11. Encyclopædia Britannica (Editorial Team). 2017. Hippocratic oath (ethical code). Encyclopædia Britannica, https://www.britannica.com/topic/Hippocratic-oath (retrieved 7/16/2017).
12. Gert, Bernard. 1998. Morality: Its Nature and Justification. New York: Oxford University Press.
13. Gert, Bernard, Charles M. Culver, and K. Danner Clouser. 2006. Bioethics: A Systematic Approach. New York: Oxford University Press.
14. Jacob, Christian P., Johannes Müller, Michael Schmidt, Katrin Hohenberger, Lise Gutknecht, Andreas Reif, Armin Schmidtke, Rainald Mössner, and Klaus Peter Lesch (2005). Cluster B personality disorders are associated with allelic variation of monoamine oxidase A activity. Neuropsychopharmacology 30, 1711-1718. Accessed 11/19/2017 at https://www.nature.com/articles/1300737.
15. Kant, Immanuel Kant. 1785 / 2002. Groundwork for the Metaphysics of Morals. Translated by Allen W. Wood, with essays by J. B. Schneewind, Marcia Baron, Shelly Kagan, and Allen W. Wood. New Haven & London: Yale University Press.
16. Rawls, John. 1971, revised edition 1999. A Theory of Justice. Oxford: Clarendon Press / Oxford University Press.
17. Resnik, David B. 2003. Is the precautionary principle unscientific? Studies in History and Philosophy of Science, Part C: Studies in History and Philosophy of Biological and Biomedical Sciences 34(2): 329-344. https://doi.org/10.1016/S1369-8486(02)00074-2 (retrieved 7/10/2017)
18. Resnik, David B., and S. S. Tinkle. 2007. Ethics in nanomedicine. Nanomedicine (Lond.) 2(3): 345-350. https://www.ncbi.nlm.nih.gov/pubmed/17716179 (retrieved 5/15/2017).
19. Sundara Rajan, Mohan. 2016. Nano: The Next Revolution, 3rd edition. New Delhi: National Book Trust.