A Review of Indian Publications on Ethical Issues Regarding Capacity, Informed Consent, and Placebo Controlled Trials

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Abstract

This paper reviews the ethical aspects of psychiatric research in India. There were a few studies on research on informed consent and capacity in psychiatric practice. Using the key words 'Consent Psychiatry India' 35 references were found in PubMed, of which 5 related to mental health. Using the key words 'Decision making and capacity India' 10 references were found in PubMed, but none were related to mental health. Using the key words: 'ethics, placebo controlled trials, India,' eight reports were found listed in Pubmed. Additional searches identified comments by editors and rapid responses. Numerous concerns were raised by the authors but these lacked evidence and were reported multiple times by same groups. Studies on informed consent report the possibility of involving patients in clinical drug trials, with valid informed consent. There is a need for more systematic studies on ethics related topics in psychiatric practice and research in India.

INTRODUCTION

Most of the research and publications on ethical aspects of research and practice has emerged from developed countries. This gives an impression that ethical principles are probably not followed in developing countries. In recent years, there has been a debate about the ethics of research in developing countries. With globalization and industrialization, multinational trials have started exploring developing countries. This seems to have created controversies, fears, and a number of reactions, mostly resisting conducting of such trials in developing countries. According to Emmanuel et al. ([1]) the controversies relate to the standard of care that should be used in research in developing countries, the "reasonable availability" of interventions that are proven to be useful during the course of research trials, and the quality of informed consent ([1]). It has been suggested that research in developing countries creates a greater risk of exploitation, and individuals or communities in developing countries assume the risks of research, but most of the benefits may be passed on to people in developed countries ([2]). Although poverty, limited health-care services, illiteracy, cultural and linguistic differences, and limited understanding of the nature of scientific research neither cause nor are necessary for exploitation, they increase the possibility of such exploitation ([2] , [3] , [4]). Recently, there were many reports and publications related to a placebo controlled trial on a group of patients with mania ([5]).

METHODS

With this background, it is important to review the research and publications in the field of ethics in psychiatric research in developing countries like India. The literature search was performed systematically by a search of the websites Medline / Pubmed, Indian Medline / Medlars, NeuroMed CD (which contains full text of the Indian Journal of psychiatry, NIMHANS Journal, and Neurology India) and an additional hand search of the Indian Journal of Psychiatry. The literature search on Informed Consent was done using the terms 'Consent Psychiatry India,' for placebo controlled trials the key words used were 'ethics, placebo controlled trials, India' and for decision making and capacity the terms used were 'Decision making and capacity India'. Only studies related to psychiatry, psychiatric practice, or mental health only were included. The cross references related to psychiatry were also sought. Those which were related to other medical disorders, general health issues, or medical practice were excluded. With regarding to the years included for the search of these databases, no limits were set. All papers published and included in PubMed were included, irrespective of the number of years. The search included more than previous ten years and was done on 29 September

2008. There were discussion papers and debates on ethical issues in psychiatry, use of modified and unmodified ECTs, child abuse etc, which have not been included in this review since these were not research based.

RESULTS

INFORMED CONSENT

Pubmed was searched using the keywords 'Consent Psychiatry India' which listed 35 citations. Of these, 5 were related to certain aspects of mental health and psychiatry, and these were included in this review [Table 1]. Ethical issues related to personal autonomy, right to information, competence, informed consent and consent by proxy were discussed in relation to ECTs ([6]) in a qualitative study. The authors suggested strategies to ensure a basic minimum standard for obtaining informed consent for ECT in India ([6]). Another paper reviewed the need for conducting an ethical inquiry in child abuse research. Ethical issues pertaining to consent and refusal, risk and benefit, effects of the study process on the researcher and the researched and the reporting of adverse events are discussed ([7]). Two papers related to ethical quandaries in anthropological fieldwork in psychiatric settings, including capacity for comprehension and confidentiality of case notes ([8]) and research on transgendered persons, where for the exploratory qualitative approach the authors took verbal informed decision and not a written consent since no medical intervention was involved ([9]). The report on management of medication noncompliance in schizophrenia by families in India by the use of concealed medications and without the patient's knowledge or consent discusses the ethical dilemmas of such a practice ([10]). The other 30 references in PubMed were either related to different medical disorders or medical practice, and were unrelated to psychiatry. A few references listed in PubMed used the words 'informed consent' for the study mentioned in the abstract, but these were not related to mental health.

Figure 1

Table 1: Publications On Informed Consent

Author	Findings / Comments
Rajkumar et al. ([6])	Ethical issues related to personal autonomy, right to information, competence, informed consent and consent by proxy are discussed. Strategies to ensure a basic minimum standard for obtaining informed consent for ECT in India are suggested.
Veena & Chandra ([7])	Core ethical concerns related to consent and refusal, risk and benefit, effects of the study process on the researcher and the researched and the reporting of adverse events. The ethical implications of the study and ethical responsibilities of the researcher are emphasized.
Addlakha ([8])	Related to anthropological field work and qualitative research. Capacity for comprehension of the research procedure and confidentiality of case notes.
Pisal & Bandewar ([9])	Exploratory qualitative approach Authors took informed decision making by participants. Written informed consent not sought as no medical intervention was involved.
Srinivasan & Thara ([10])	Role of concealed antipsychotic medications for those refusing treatment and non-compliant is discussed. Cultural appropriateness and ethical issues of this method are discussed as family members are main caregivers.

Some interesting reports throw light on the understanding, perception and application of informed consent in psychiatric research. In a study on informed consent on participants in a double blind drug trial, it was reported that except for 2 out of 275 participants, all participants expressed clear choice, 62% consented; 37% refused for various reasons, 15% asked more information before deciding and consenting, while only 2 expected the doctor to decide for them. Non consenting did not differ on the basis of education, gender, socio economic status, or clinical features ([11]). It was further observed that 40% consented without asking questions, 12% asked more details and consented, 3% asked more details and do not consent, 10% refused due to possible risk, 10% refused due to inability to follow-up, and 24% refused due to long distance ([11]). Although the stereotype is that people from an underprivileged background cannot comprehend the components of informed consent, these studies show that a patient's level of understanding is related to the amount of information that is provided rather than to their background characteristics.

Another study focused on the Neurology professional's views of difficulties in obtaining consent. The difficulties were reportedly perceived to be due to illiteracy of patients or volunteers (70%), patients' inability for regular follow-up (56%), patients' expecting doctors to decide (51%), patients' refusal due to possible risk (33%), patients' inability to differentiate therapeutic and research settings (31%), and difficulty in explaining the risks 23% ([12]).

A study on the proportion of published psychiatric research

where informed consent and ethical approval were reported noted that consent was obtained in 45% of the published studies, which was inadequate and unwritten in most studies. The approval of the local ethics committee was not mentioned in most studies, including some studies involving drug trials ([13]).

DECISION MAKING AND CAPACITY

Using the search terms 'Decision making and capacity India,' 10 references were cited in PubMed. None were related to mental health or psychiatric practice. These references related to malaria, HIV, family planning, organ donors, or health policies.

In the Indian setting, decision making is influenced by psychiatric patients and their families who may not accept that the patient has psychiatric illness, hence there is no question of consent for treatment. Many patients and relatives may feel that their patients are ill but not from a psychiatric illness. Therefore, use of psychotropic drugs may not be acceptable to them. Some may agree that they have psychological problems but they need to control it themselves without drug treatment. Others may feel that the problems are supernatural and need medico-religious treatments. Some others may have prejudices against psychotropic drugs and ECT and may not agree to give consent ([14]).

In a study on the treatment related decision making capacity in psychotic inpatients, of 63 patients, 64% had a lack of capacity. This lack of capacity was associated with low education, lack of employment, high level of psychopathology and cognitive dysfunction. On the other hand, 23% of involuntarily admitted patients had capacity present at the time of interview and 41% of patients who were voluntarily admitted had a lack of capacity ([15]).

PLACEBO CONTROLLED DRUG TRIALS

In view of the controversies surrounding ethics of placebo controlled clinical trials in psychiatry in developing countries, a systematic review methodology was employed with an aim to evaluate the evidence regarding perception of ethics in psychiatric research, especially placebo controlled trials, in India. The keywords used for the literature search were in this area were 'ethics, placebo controlled trials, India.' Once all possible study reports were identified and collected, each publication was assessed for reported findings.

Using the above key words, eight citations were found in Pubmed. Further, there were two comments by editors and a few eletters or rapid responses in related journals. There were no research based reports. All publications were commentaries or letters to editors or correspondence. All but one were related to a recently published article on a placebo controlled trial ([5]). All articles were extracted, read, summarized, and tabulated in Table 2.

Figure 2

Table 2: Publications On Placebo Controlled Trials

Author	Findings / Comments
Tharyan [25]	Genuine uncertainty regarding some of the controversies that surround the science and ethics of RCTs and the need for more systematic and culture-specific quantitative and qualitative research to inform the design of future trials
Patel [17]	What new information does this trial add that justifies the trial in the first place? Is there an ethical basis for a placebo-controlled trial in severe mania? How was signed informed consent obtained from such severely ill manic patients Was there any financial transaction between the authors and the drug company? Was there IRB approval for this trial?
Srinivasan et al.[16] Thomas [25]	Why was the study done? Why was a placebo used when an effective treatment exists? How did patients give informed consent? Where were the trial sites? Who were the participants and what quality of care did they receive? What were the adverse events? Was the 'wash-out' period medically and morally justified? Do the other authors have any competing interest to declare? In what sense was the trial conducted according to the Declaration of Helsinki?
Murtagh & Murphy [18]	Why was there no discussion about the ethical dilemmas associated with this study?
Basil et al.[19] Basil et al [26]	Concerns about the legitimacy and validity of the informed consent obtained from patients with acute mania Concerns about placebo control
Mudur [24]	Commentaries of above with responses of the investigators
Geller et al.[33]	Maintaining ethical principles in the conduct of research in developing nations
Khanna [20] Khanna [21] Tyrer [22] Tyrer [27]	Response to comments Opinion in BJP/ BMJ

Numerous concerns were raised by the authors. Multiple submissions by individuals or groups were noted. There were comments in the letter by Srinivasan et al. ([16]), stating '…this trial could not have been conducted in a high income country…' which were not evidence based. A literature search done to verify this statement found 20 placebo controlled trials on different groups of psychiatry patients with psychosis, mania, schizophrenia, and depression published in different leading international Psychiatry journals conducted in the developed countries within the last 3 to 4 years. None were actually conducted only in a developing country. Another commentary ([17]) had many similarities with the letter published by Srinivasan et al ([16]). Similar questions were raised in both publications, raising doubts about originality. Other eletters [in BJP online] ([18] , [19]) in response to the article from different parts of the world raised other different issues.

Khanna's ([20] , [21]) responses are similar in both the journals, which is expected as similar questions were raised. The comments of the editor ([22]) further add to repetitive publishing. It was also noted that some of the authors of these commentaries / correspondence had also submitted comments as BMJ rapid responses.

Tharyan ([23]) provided evidence for and against placebo controlled trials with supporting literature. The issues were highlighted in the news section of the BMJ ([24]) as well which led to the repetitive rapid responses ([25] , [26]) from authors who had already sent their comments to other journals for publication. More concerns were raised about discussion of the ethical dilemmas associated with this study ([25]), and legitimacy and validity of the informed consent obtained from patients with acute mania ([26]).

DISCUSSION

A number of areas related to ethics, like confidentiality and privacy, have not been studied or discussed in the Indian literature, though these might be of relevance and importance. The studies on informed consent have revealed that it is possible to obtain informed consent for drug trials, although the process is complex when seeking consent for treatment of psychiatric disorders.

The persistence of controversies on placebo controlled trials suggests that existing ethical guidelines can be interpreted in different ways, are sometimes contradictory, or rely on unstated, yet controversial, ethical principles ([1]). Although numerous concerns were raised by the authors in the literature search, on close examination many concerns were not evidence based. For example, the literature search to verify the statement that such placebo controlled trials could not have been conducted in a high income country, found the contrary. Similarly, seeking informed consent for a drug trial was not found to be a problem ([11]). It seems that members of the same team published similar matter in different journals ([16] , [17] , [25]). It is difficult to classify this type of duplicate publishing. Similarly, dual publications were noted for other authors ([19] , [26]), response by authors ([20] , [21]) and editor of a journal ([22] , [27]). The reason for this is difficult to speculate, but may be a reflection of their great concern about exploitation of the patients or the situation in developing countries ([23]).

In countries where little research has been done on ethical aspects, the discussion about the ethics of clinical trials in India appears misleading. It is difficult to understand the motives which generate such a controversy and force authors to republish their views, especially if these are negative. It can be interpreted in two ways. One is to reflect the great concern of these individuals. On the other hand, perhaps there is some conflict of interest or moral identity where those who view themselves as moral individuals pursue possibly extreme alternatives ([28]). The authors are forceful and repetitive in voicing their concerns even using possible misinformation. The merit and importance of clinical trials to be conducted in developing countries is hardly discussed. As of now, many clinicians in developing countries use results from trials conducted in developed countries for their patients. This may not be the most appropriate way to help their patients. However, this approach is possibly occurring due to the lack of better alternative evidence.

Some other areas of ethical importance, which have been discussed and debated are related to the use of electroconvulsive therapies, including unmodified ECTs ([2930]), and the ethical issues related to indigenous models of mental health services ([31]). Wig ([32]) has discussed that in India where a large number of patients are poorly educated, giving consent by signing some research protocol may be an inadequate safeguard. The patients and their families inherently trust their doctors and hence a big ethical responsibility falls on the treating doctor. However, a complete ban on all research on the mentally ill may be going to the extreme. Two safeguards are suggested. First, such research should be strictly limited to what is in the larger interest of the mentally ill. Second, there must be independent monitoring to ensure that ethical guidelines are followed ([32]). Routine use of structured assessment of capacity to consent before recruiting the patients into research studies or RCTs may be an acceptable method, however, there are no locally developed scales or instruments. There is a need to develop locally relevant and culturally sensitive structured assessment tools to assess capacity to consent and appropriate guidelines for seeking informed consent.

CONCLUSIONS

There is a need for more research on different ethics related themes in psychiatric settings in India. More research is required on the process of seeking consent for treatment and research, assessing capacity, confidentiality, privacy and making choices. It can be suggested that debates and controversies over placebo controlled trials in developing countries have been blown out of proportion.

References

1. Emanuel EJ, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? the benchmarks of ethical research. J Infect Dis 2004;189:930-937.
2. Benatar SR. Avoiding exploitation in clinical research. Camb Q Health Ethics 2000;9:562-565.
3. Wilmshurst P. Scientific imperialism: if they won't benefit from the findings, poor people in the developing world shouldn't be used in research. BMJ 1997;314:840-841.
4. Shapiro H, Meslin E. The ethics of international research. N Engl J Med 2001;314:139-142.
5. Khanna S, Vieta E, Lyons B, Grossman F, Eerdekens M, Kramer M. Risperidone in the treatment of acute mania: double-blind, placebo-controlled study. Br J Psychiatry 2005;187:229-234
6. Rajkumar AP, Sarvanan B & Jakob KS. Voices of people who have received ECT. Indian J Med Ethics 2007;4:157-164.
7. Veena AS, Chandra P. A review of the ethics in research on child abuse. Indian J Med Ethics 2007;4:113-115
8. Addlakha R. Ethical quandaries in anthropological fieldwork in psychiatric settings. Indian J Med Ethics 2005;2:55-56
9. Pisal H. Bandewar S. Research with transgendered people. Indian J Med Ethics 2005;2(1):22-23.
10. Srinivasan TN, Thara S. At issue: management of medication noncompliance in schizophrenia by families in India. Schizophr Bull 2002;28:531-535.
11. Murthy RS, Chatterjee S, Sriram TG, Shetty M, Raghavan KS. Informed consent for a drug trial : a systematic study. NIMHANS J 1988;6:145-149.
12. Chatterjee S, Varghese M, Jain S, Raghavan KS. Ethical issues in medical research: an opinion survey of neurologists and neurosurgeons. Neurology India 1989;37(3):249-254.
13. Somashekar BS, Chaturvedi SK. Informed consent in published psychiatric literature in India. Indian J Psychiatry 2002;44:54.
14. Agarwal AK. Ethical issues in practice of psychiatry. Indian J Psychiatry 2001:43:18-25.
15. Gandhi Z, G. K. Vankar GK. Treatment related decision making capacity in psychotic inpatients. Indian J Psychiatry 2007;49:66-67.
16. Srinivasan S, Pai SA, Bhan A, Jesani A, Thomas G. Trial of risperidone in India--concerns. Br J Psychiatry 2006;188:489.
17. Patel V. Ethics of placebo-controlled trial in severe mania. Indian J Med Ethics 2006;3:11-12.
18. Murtagh A, Murphy KC. Trial of risperidone in India--concerns. Br J Psychiatry 2006;188:489.
19. Basil B, Adetunji B, Mathews M, Budur K. Trial of risperidone in India--concerns. Br J Psychiatry 2006;188:489-490.
20. Khanna S. Response to Dr Vikram Patel. Indian J Med Ethics 2006;3:17-18.
21. Khanna S. Author's Response. Br J Psychiatry 2006;188:490-491.
22. Tyrer P. Editor's reply. Br J Psychiatry 2006;188:490-491.
23. Tharyan P. Placebo-controlled trials in psychiatry on trial. Indian J Med Ethics 2006;3:13-16.
24. Mudur G. Indian study sparks debate on the use of placebo in psychiatry trials. BMJ 2006;332:566.
25. Thomas G. Report leaves questions unanswered. Rapid Response bmj.com 17 March 2006. http://www.bmj.com/cgi/eletters/332/7541/566-a#130031 . Accessed on 29 October 2008.
26. Basil B, Mathews M, Adetunji B, Budur K, Mahmud J, Chakraborti I. Placebo trials in developing countries. Rapid Response bmj.com 17 March 2006. http://www.bmj.com/cgi/eletters/332/7541/566-a#130031 . Accessed on 29 October 2008.
27. Tyrer P. Placebo trials in India. Rapid Response bmj.com, 20 Mar 2006. http://www.bmj.com/cgi/eletters/332/7541/566-a#130031 .Accessed on 29 October 2008.
28. Reynolds, Scott J, Ceranic TL. The effects of moral judgment and moral identity on moral behavior: an empirical examination of the moral individual. J Appl Psychol 2007;92:1610-1624.
29. Andrade C. Electroconvulsive therapies- a measured defense. Indian J Med Ethics 2003, 11(2):44-46.
30. Andrade C. Unmodified ECTs. Indian J Med Ethics 2003;11:9-10.
31. Tharyan A. Mental Health Services – indigenous models of care in community. Indian J Med Ethics 2008;5:75-78.
32. Wig NN. Ethical issues in psychiatry. Indian J Med Ethics 2004;12(3):11-12.
33. Geller SE, Patel A, Niak VA, Goudar SS, Edlavitch SA, Kodkany BS, Derman RJ.. Conducting international collaborative research in developing nations. Int J Gynaecol Obstet 2004;87:267-271.

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