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Short Communication

Statistics Section

Some Objectivity to the Ethical Aspects in Conduct of Clinical Research in Vulnerable Population

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ABSTRACT

Vulnerable population is one of the important parts of our population which also need to be benefited from the results of clinical research. In view of their limited autonomy it may not be easy to conduct clinical research such as clinical trials in them because of ethical issues. When it is must to conduct clinical trial in this population, along with ethical considerations, some statistical and clinical research issues may also be addressed to give the objectivity to the decision of conducting trials in this population, which is not in a position to convey their acceptance of participating in the trial independently. The paper discusses the issues in vulnerable population through the concepts in clinical research and some objective ethical considerations before arriving at the decision of conducting a clinical trial.

Keywords: Clinical trial, Effect size, Ethics

INTRODUCTION

Vulnerable population are those groups of population who bear unequal burden of research because of their easy availability in the settings where the research is being conducted [1,2]. This type of population includes prisoners, children, pregnant women and subordinate employees in an organisation [3]. There is possibility of them being research participant under compulsion because of less autonomy. It is also expected from the research system that the benefits and risks are equally distributed among all sections of population and rights of vulnerable population are protected [4]. There is obvious need to have well-defined ethical principles which currently ICMR guidelines provide in India [5]. This is based on the basic principles of respecting an individual under the conditions of limited autonomy because of mental health issues or being under pressure, such as prisoners etc. Hence, it may be stated that the studies may be taken up in such population when it is must. This "must" have to be defined or quantified. This is the process of further strengthening the ethical principles. In other words, studies in vulnerable populations are justified only when research could not be carried out well with less vulnerable population.

The aim of this article is to address the issues of vulnerable population considering objective ethical aspects, so that an effort could be made to quantify the conditions under which the study such as clinical trials, on vulnerable population is to be conducted. This includes the justification that study is must and not being conducted because of the easy availability of the participants. It needs to be ethically or statistically seen, in terms of "must" through some objectivity. This objectivity can be seen in terms of anticipated substantial benefit from the proposed intervention which can be seen through effect size with minimum burden (sample size) as indicated by ethical principles in such studies. It has been generally indicated in number of studies that due caution in designing and conduct of studies in the vulnerable population is needed. This includes comprehensive data safety monitoring board strict supervision for observing norms advocated by Institutional Ethics Committee and built-in mechanism for interim statistical analysis if indicated [6]. This article tries to address specific issues in research on vulnerable population which need to be seen in statistical perspective so as to help the study planners and program people to make decisions, based on some quantified facts keeping in line with the standard ethical and Good Clinical Practice (GCP) guidelines.

Ethical Considerations

According to Helsinki declaration, the study in vulnerable population is justified if the research is responsive to the health needs and priorities of that population [7]. This is with a reasonable expectation that community benefits from the research conducted on them. This could be also expressed in terms of clinical research by stating that the study in the population with limited autonomy should be conducted only when the intervention in question has a likelihood of giving a substantial benefit to the group. This could be objectively considered as the "effect size" in clinical research [8].

When we say expected effect size is higher than we expect in other population with more autonomy then the sample size computed will be less in special group than the other population for the fixed type 1 and type 2 errors. It means minimising the burden on this special group and making the benefit available to the larger group.

This would provide objectivity to the situation for deciding on the conduct of the study in this special community (vulnerable). The expert group would decide on the magnitude of the expected benefit (effect size) and could be one of the objective considerations for the conduct of the study, following the standard ethical guide lines. The researcher should consider a defined threshold of effect size only beyond which the study should be indicative. This would turn out to be natural ethical advantage for conducting study in less autonomous population.

It is also important that we do not miss on the likely substantial difference between the new interventions and standard comparator or treatment particularly in vulnerable population. Since we have ventured into studies in vulnerable population, we do not want to miss on the real effect if it exists. This can be done by maintaining the power in the study of reasonable good size. Most common approach to increase the power is to increase the sample size but in this situation (vulnerable population) might be difficult considering the principle of minimal burden on less autonomous population. Conventionally, magnitude of chance factor which is type 1 error is maintained at 0.05 or less so as to minimise the chance of wrongly rejecting the null hypothesis. This obviously minimises the risk of inappropriate consideration of the effect size as significant. But in some limited conditions where intervention under consideration has minimum side effects or treatment options are limited one could consider an option of liberalising type 1 error in vulnerable population

where the studies are not taken up easily for the ethical reasons of limited autonomy, so as to provide enough opportunity for the new options of treatment being expressed (increasing power without additional burden of increasing sample size) [9]. Of course this could be discussed among the experts on the subject members of IRB who are well familiar with the objectives of the research before the start of the study.

CONCLUSION

The above discussed considerations would help health researchers to decide on the conduct of research in vulnerable population more objectively and ethically.

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