Ethics Behind Clinical Trials Involving Children

Clinical trials provide various aspects of understanding about drug safety and are critical steps for drug development. However, there are less research done in pediatric subjects than adult subjects because of ethical concerns, funding, and methodology to conducting the clinical study. The lack of clinical trials in children lead to ineffective medicines and unknown side effects that increases risks for children and stems from extrapolation of clinical trial results in adults. This is a problem because some diseases are only prevalent in children and because children are physiologically, developmentally, and psychologically different than adults.

Phase I clinical trials are the preliminary study of safety and pharmacokinetics on human subjects. This round of testing is discouraged in children because of the unknown side effects that can arise. Unless standard practices have failed and the child subject suffers a life-threatening condition, Phase I clinical trials are usually tested in adults after rounds of animal testing. This is more acceptable because of ethical concerns like individual consent and liabilities of the subject rather than parental consent. Phase II clinical trials assesses safety and efficacy and occasionally uses pediatric subjects. Phase III studies are used to understand the efficacy, acceptability, and adverse effects of drugs which is compared to standard therapies and usually involve the use of a placebo. These trials try to limit testing on children to refrain from exposing children to unnecessary harm. Lastly, post-marketing trials (Phase IV) are infrequently tested in children even though the Federal Drug Administration and Pediatric Research Equity Act requires pediatric trials on marketed drugs. The lack of testing in pediatric subjects also is linked with the small sample size of the studies due to lack of recruitment. Underpowered trials consist of a small sample size and provide inconclusive results and preventable waste of resources and efforts. Publicity of trials can prevent factors like improving transparency for greater confidence

from both patient and investigator, duplicative studies to limit unnecessary harm, and bias of incomplete or poor results and even unpublished results. By increasing accessibility, pediatric clinical trial results can be introduced to clinical practices and the results would improve public trust and confidence in both the medicine and the advocate the use of children in clinical trials.

Children of different developing age groups may cause the medication to have dissimilar effects which involve pharmacokinetic studies. Therefore, testing of different pediatric age ranges are needed to supply the most appropriate dose and provide better care for pediatric patients. Challenges surrounding the studies involve the lack of expertise in analysis of results in children, quantitative sampling techniques like a small sample size, and the lack of micro-analytical techniques of drug concentration in small specimen. To combat this, new approaches are developed for pharmacogenomic techniques and use of sampling to gather better results to understanding the pharmacokinetics of medicines in children.

The goal of protecting children from risk of untested medicine creates ethical concerns that involve reluctance of parents and doctors to participate in clinical trials. Parents have a societal role to give consent and to make the decision for their children. This consent is determined by personal values, the child's condition, and the trial type. Informed consent should be provided and understood by all parties as tailoring research to the consented procedure of the trials allows for respect between the parents and the investigators. Consent from the children is also an important factor as it makes it more ethical for children to participate in clinical trials when all parties understand the risks and benefits in appropriate ways. Payment in normal clinical trials, and is categorized by reimbursement, compensation, appreciation, or incentive. This is a concern as it can entice or distort the judgement involving risks to the child, but a lack

of reimbursement or compensation may cause unnecessary financial struggles. To combat this, committees must ensure the fair participation with reasonable compensation.

To make clinical trials more ethical, investigators must take into account the methodology by which the procedure is carried out. Children's aversion to needles, for example, should be considered when determine the method of administration. However, not all drugs are fully effective when administered differently. Therefore, the need for trained investigators that can tailor the clinical trial to children and curate accurate reports from children increases the difficulty of testing in children. Collaboration between various committees and groups can provide a central database leading to auditing of Good Clinical Practices as well as protocol development in testing with pediatric subjects. The next steps would be to obtain greater advocacy and investment to fuel evidence-based treatment for children.

I believe that children should participate in clinical trials because it increases the research for the medicine and the disease for children. Children take medications and understanding the risks specific to children can prevent mishaps like the Thalidomide incident. On the other hand, increased recruitment has been seen in cancer studies in children because of the high threat and need for hope that entice the study of cancer on children. However, specific safety measures should be established when studying clinical trials on children like the consideration of routes of administration and appropriate methods of obtaining consent through transparency. There are also different techniques of acquiring accurate reports in young children because of communication due to developmental abilities. Examples can be observing and using quality of life data from both the child and the parent to assess the results or using the face-pain scale as a reference to the results. Well informed practitioners can decrease the reluctance of participation as a study shows that parents tend to trust their doctors and acknowledge that the doctors would

not approach the parents about research if it jeopardizes the safety of the child. Payment from clinical trials should be regulated in clinical trials as it should not entice the consent for participation. Payment should be more regulated with pediatric subjects because the consent and decision is made by the parents, even though the child would have consented too. I would agree that necessary compensation should be awarded but possibly that the clinical trial need to be referred by a practitioner. The ability to fund the clinical trials is important to be able to conduct the clinical trials. However, high market value medicines that are usually used in adults have a greater incentive for funding than the market value of medicines that may be off patent for children. Therefore, private funding may be sought to conduct those clinical trials. Collaboration between pharmaceutical companies, organization, and research provide good ways to audit protocols and to further instigate safety in clinical trials.

Bibliography

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