Clinical Obstetrics, Gynecology and Reproductive Medicine

Research Article

Perceptions of Saudi parents on the participation of their infants in clinical research

Saleh Al-Alaiyan[1]*, Ahlam AlSanad[1], Hani Al-Ali[1], Magdy Dawoud[1], Fahad Al-Hazzani[1], Khalid AlFaleh[2], Eyad AlMidani[1] and Emad Khadawardi[1]

[1]Department of Pediatrics, Neonatology Section, King Faisal specialist Hospital & Research Centre, Saudi Arabia

[2]King Saud University-Riyadh, Saudi Arabia

Abstract

Objectives: To examine attitudes of Saudi parents about doing research on their infants.

Subjects and methods: Fifty eight parents of newborn infants in the neonatal intensive care unit (NICU), and 42 parents of the normal newborn nursery (NNN) returned completed questionnaires. The survey included questions with graded responses and five research scenarios with different levels of risks and benefits. Statistical analysis included Chi square analysis and Fisher's exact test were used to determine a difference between the two groups in responses to scale items.

Results: We found that parents showed generally favorable attitudes toward research with infants. Comparisons between the two parent groups revealed a significant difference ($p<0.05$) on just one item which showed that the NNN group had a good understanding of the way research was conducted. There were no statistical differences in the five scenarios except in scenario that parents in NICU were significantly more likely to enroll their infants in research. There was an agreement; with few exceptions, parents wanted to be asked for consent and would like to make decisions by themselves.

Conclusion: Parents included in this study understand the importance of doing research even they are in agreement in enrolling their own infants in studies that are risky but they want to be consented before commencing any research.

Introduction

Good neonatal research is essential because it improves the care and outcome of newborn infants. Vital research in newborn infants may be being stifled through misplaced fears of causing parents stress by asking them to permit their infant's entry into clinical trials.

To improve pediatric medical care, it is important to perform research studies and interventions with children that do not offer a compensating potential for clinical benefit [1-3]. Guidelines around the world allow children to be involved in such nonbeneficial research when the risks are minimal [4-6].

Research on newborns may not be allowed by parents, unless there is a possibility that they will benefit directly from the research. On the other hand, risky research may be permitted by parents only on sick newborns who might result in therapeutic benefit. Some researchers reached to a conclusion that many parents do not adequately understand clinical research. Parents and children often fail to understand randomization, especially as it relates to the principle of clinical equipoise. Children have additional difficulty with the nature of placebos and with right to withdraw from research at any time. Future research should prospectively evaluate interventions such as "staged consent," public education, medical trainee education, and alternative information-delivery methods, which are not yet known to consistently affect understanding. This could explain why many clinical trials suffer poor enrollment rates, studies may be canceled, take much longer to conduct, or fail to answer the research question [7].

In a similar study [8] that showed that parents generally had favorable attitudes toward research with infants. The authors found that there was a trend toward more trust in doctors by "NICU parents." Parents with newborns in NICU were significantly more likely to enroll their newborn in a study involving moderate risk and possible major direct benefit. They found that almost a third of the sample in both groups was willing to enroll their newborn in a study with moderate risk and no direct benefit.

Despite the wealth of clinical research that has been conducted on this population, gaps still exist in our knowledge of parental attitudes around research with newborn infants. Given the ethical sensitivity of research with this population, and the need to minimize harm for parents and infants, more studies are needed to ensure the integrity of the consent process.

To the best of our knowledge, the perception of Saudi parents of research with their infants has not been studied. We believe that this study will shed light on the attitude of parents when their infant is intended to be enrolled in research. Unfortunately, some of the clinical research performed in some institutions does not follow the international regulations; however, some may be performed without

Correspondence to: Dr. Saleh Al-Alaiyan, Department of Pediatrics (MBC-58), King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia, Tel: +966-1-442-7761; Fax: +966-1-442-7784; E-mail: alaiyan@kfshrc.edu.sa

Key words: *newborns, infants, research, parents, informed consents*

Received: September 20, 2016; **Accepted:** October 06, 2016; **Published:** October 10, 2016

consenting parents.

Aim of the study

The aim of this study is to examine the following:

1. The acceptability of parents to perform research with their infants,

2. Their understanding of research-related risks that they accept if their infant is enrolled,

3. Differences in beliefs between parents of sick and well newborn babies as well between mothers and fathers of newborn babies and finally

4. The relationship between parents' education and attitudes towards research.

Subjects and methods

The study were conducted at Neonatal Intensive Care Unit and the Normal Newborn Nurseries of King Faisal Specialist Hospital & Research Hospital-Riyadh, Saudi Arabia (KFSH & RC). The number of deliveries at our hospital is around 1500-1800 per year and almost 30% of delivered babies are admitted to our NICU. In addition, we accept infants delivered outside our hospital to give a total of 500-600 admissions per year. Volunteer subjects were parents of newborn babies in the intensive care (NICU-group) and normal newborn nurseries (NNN-group). The instrument used in this study included questions (35-item questionnaire) with graded responses and five research scenarios with varied risks and benefits. The questionnaire used in this study is the same one used by Oberle K *et al*. [8,9] with a permission that was obtained from the correspondent author Dr Nalini Singhal. Content and face validity of this questionnaire were established by an expert panel and a pilot test conducted with a small group of health care professionals and lay persons.

The questionnaire included demographic questions; scaled items about research with newborn babies; scenarios describing research studies that varied in degree of risk and benefit to the newborn baby; questions about parents' willingness to enroll their newborn baby in the studies described; and questions regarding circumstances under which consent should be sought.

One of the investigators will assess the parents to identify who might qualify for the study, and they will be enrolled if they are not felt to be unduly stressed. Similarly, parents of normal newborns will be approached. Both parents will be given the questionnaire and they will be reminded to return it within three days.

Data collection

The questionnaire used in this study is composed of four parts that contain 35-items. Part A requests demographic information. Part B consists of 18 Likert-type questions designed to explore parents' beliefs about the following themes: acceptability of research on infants, trust in doctors, parents as decision makers, consent for research, and research personnel. Participants will be asked to rate their level of agreement to statements on a five-point scale ranging from "strongly disagree" to "strongly agree."

Part C consists of five scenarios designed to determine the kinds of studies in which parents would be likely to enroll their infants, and circumstances under which they would prefer to be asked for consent. The scenarios are constructed to represent typical studies that might be carried out in the NICU:

Scenario (1) Little, if any, increased risk to the infant, minor discomfort, and possible direct benefit. Imagine your baby is well but has an intravenous catheter to give fluid and we have different procedures to fix the catheter to secure it that we want to test to avoid slipping out. There will be little, if any, risk to your baby and there will be a possible benefit.

Scenario (2) Little, if any, risk to the infant, minor discomfort, and no direct benefit, but a possibility of longer-term benefit to others. Imagine your baby is well but we need to get blood from his vein to do genetic studies. There will be little, if any, risk to your infant and minor discomfort but no direct benefit to your baby.

Scenario (3) A very small probability of major risk to the infant, some discomfort, and no direct benefit, but a possibility of longer-term benefit to others. Imagine that your baby is having some trouble breathing. A catheter (small tube) will be inserted into the blood vessel supplying the baby's lungs. We will use the catheter to measure pressures in the baby's lungs. Knowing the pressures in the vessels in the lungs in different diseases will help other babies in the future. It will not help your baby directly. There will be some discomfort to your baby when the catheter is inserted. There is also a very small risk of infection and that the catheter could cause serious bleeding from the major blood vessel.

Scenario (4) Moderate risk to a sick infant, little or no discomfort, and possible major benefit. Imagine your baby is sick with lung disease and he/she is on an artificial ventilation and we need to test the effect of an investigational drug that will be aerosolized and inhaled by your baby. The study is placebo-controlled trial which means that your baby either receives the drug or placebo. The purpose of the drug is to enhance lung compliance. There will be moderate risk to your sick baby, little or no discomfort, and possible major benefit.

Scenario (5) Major risk to the infant and potential for major benefit. Imagine your baby is very sick and he/she has to be offered a new combination of drugs that might be lifesaving, but which would have numerous and severe side effects. There will be a major risk, including death, to this very sick baby, but potential for major benefit.

Part D of the questionnaire consists of one open-ended question in which parents will be asked to make any comments about research with newborn babies, or about the process of getting consent from parents for research.

Data analysis

The study was approved by the ethics committee at KFSH & RC. Statistical analysis included Chi square analysis and Fisher's exact test were used to determine a difference between the two groups in responses to scale items. Quantitative data were entered into a computer database, checked, and analyzed using SPSS. Descriptive statistics were calculated on all demographic variables. The statistical level of significance is set at $p<0.05$.

Results

One hundred parents returned completed questionnaires (NICU-group 58 & NNN-group 42) (Table 1). There were 47 males and 53 females, GA (weeks); median 34 (24-40), age of mother(Y); median 31.5 (18-45), and age of father (Y); median 37 (23-53). The level of education showed that 92% had high school and some college or university. Ninety percent of parents in NICU and 88% in NNN group

Table 1. Responses to scaled items by NICU and NNN group.

Item	% agree (NICU), n=58	% agree (NNN), n=42	P value
Acceptability on research on babies			
Research should be carried out on babies	67	71	0.872
I would never consent to have my baby in research study	74	57	0.335
It is wrong to do research on babies because they have no say in the matter	62	54	0.961
research to me means that my baby is being used as a guinea pig	34	33	0.156
Research must be done on some babies for the good of all babies	76	69	0.879
Even if babies are put at some additional risk, I think it is important to do studies to improve the quality of care for future babies	52	32	0.223
Trust in doctors			
I trust my doctors and if he/she suggested I should put my baby in a research study, I would agree	74	67	0.210
I trust that doctors at this hospital would not ask to do research that would put babies in real danger	86	86	0.997
Parents as a decision makers			
Parents should have the chance to keep their babies out of research if there is any risk to the baby, even if the research is the only chance a baby has for a certain treatment	71	67	0.074
I have a good understanding of the way research is conducted	65	78	0.039*
Consent for research			
All forms of research with babies, no matter how minor, should be carried out only after parents have given informed consent	96	98	0.459
Parents might accept a certain research risk for themselves, but they do not have the right to accept that risk for their babies	74	81	0.381
It is not necessary to ask the parents for consent for minor procedures just because they are part of a research study	22	26	0.225
Doctors should make the decisions about which babies should be in research; I do not think the parents should have to make the decision	15	26	0.442
To collect information for the important of health care; certain confidential information from patient's' chart could be looked at without consent----- the information obtained must be kept confidential	79	78	0.511
Research Personnel			
Research should be done by doctors only (not nurses or other health professional)	83	86	0.441
Evaluating research			
The public needs more information about research with sick babies	90	93	o.785
There is a approval process for research that makes sure are not harmed	90	98	0.315

*Statistically significant

never worked in health care. We found that parents showed generally favorable attitudes toward research with infants. Comparisons between the two parent groups revealed a significant difference ($p<0.05$) on just one item which showed that the NNN group had a good understanding of the way research was conducted. There were no statistical differences in the five scenarios except in scenario (3) where parents were in favor of enrolling their infants in research. Although there was no significant statistical differences but parents in both groups agreed that they trust doctors at this hospital and they know that they would not ask to do research that would put their infants in real danger. There was overwhelming agreement; with few exceptions, parents wanted to be asked for consent and would like to make decisions by themselves.

Discussion

We found that parents showed generally favorable attitudes toward research with infants. The majority of parents in both groups never worked in health care. Moreover, parents of infants in the NNN group had a good understanding of the way research was conducted in comparison to the NICU group. This understanding may be related to the level of education as we found that the majority of parents had high school and some college or university. We found that there was overwhelming agreement among parents regarding consents prior to research and they would like to make decisions by themselves. The answers of parents regarding the five scenario showed that they were in favor of enrolling their infants in research. Majority of parents stated that they trust doctors in conducting research in their infants because they understand that they would not ask to do research that would put their infants in real danger.

Several studies from developed and developing countries explored factors that influence parental acceptance or refusal of having their infants enrolled in clinical research. In a study from Lebanon [10] showed benefit/risk ratio assessment was a major determinant of parental consent. Authors found that fear of adverse events or painful procedures in research was a recurring theme in most interviews. Whereas perception of direct benefit to the child, trust in the physician or institution, financial gains or having a positive previous experience in research facilitated consent. Nevertheless, they stated that a complex informed consent form and misunderstanding of the term 'randomization' hindered parental approval of participation. In a study that was conducted in Egypt [11], found several factors that influence parental consent for participation in clinical research involving children in Egypt. The study found that factors favoring consent were: research of benefit to child, and enough explanation about the benefits that can be gained from the research. In addition, the study explored factors favoring refusal which were: use of new drugs or vaccines and invasive procedures.

High level of education is important for communication but it can be a reason favoring refusal of parents to have their infants participating in a clinical research. In a cross-sectional survey [12] conducted over

3 years period found that parents who graduated from college and private health insurance were associated with a lower likelihood of providing consent. Furthermore, parents who perceived the trial as having a low degree of risk, resulting in greater benefit to their child and other children, causing little interference with standard care, or exhibiting potential for enhanced care, or who perceived the researcher as professional were significantly more likely to consent to participate. Higher levels of understanding of the randomization process, blinding, and right to withdraw were significantly positively associated with consent to participate.

It is not always that parents are satisfied by the informed consent given to them to sign prior to enrolling their infants in a clinical research. In a recent systematic review, authors concluded that despite a variety of opinions among parents and clinicians there is a strongly and widely held view that it is important that parents do give or decline consent for neonatal participation in trials. They added that none of the range of existing consent processes reviewed by the research is satisfactory [13].

It appears that better communication between physicians and parents prior to enrolling their infants in a clinical research is essential in recruitment. In an audio-recorded trial [14] that recorded discussions between practitioners and parents reached to a conclusion that parents were overwhelmed with information that resulted in misunderstandings. They stated that parents had many questions and concerns about trial participation which influenced their decision-making, they rarely voiced these during discussions about the trials with practitioners, which had the potential to influence their decisions. Some trials with complicated designs that necessitate to enhance explanation with emphasis on the ethical considerations that make parents understand that the trial involvement is voluntary and it is different from routine care and that they could withdraw from the trial at any time [15]. Adequate time is required for parents to decide about research participation is associated with their willingness to enroll their child in research [16].

Consideration of all factors that influence the decision of parents including better communication with enhanced explanation and the quality of the informed consent process may improve participation in pediatric clinical trials.

Conclusion

Parents included in this study understand the importance of doing research even they are in agreement in enrolling their own infants in studies that are risky but they want to be consented before commencing any research. Better communications with parents, building trust between doctors and parents and obtaining informed consent are essential in improving recruitment.

References

1. Institute of Medicine (2004) Ethical Conduct of Clinical Research Involving Children. Field MJ, Behrman RE, eds. Washington, DC: National Academies Press.
2. Roberts R, Rodriguez W, Murphy D, Crescenzi T (2003) Pediatric drug labeling: improving the safety and efficacy of pediatric therapies. *JAMA* 290: 905-911.[Crossref]
3. Caldwell PH, Murphy SB, Butow PN, Craig JC (2004) Clinical trials in children. *Lancet* 364: 803-811.[Crossref]
4. Department of Health and Human Services Office of Human Research Protections. Code of Federal Regulations: Title 45, Part 46, subpart D. Revised June 18, 1991.
5. Food and Drug Administration. FDA Regulations: Protection of Human Subjects.
6. 21 CFR 50, subpart D: Additional Safeguards for Children in Clinical Investigations. Revised 2002.
7. Oelstrom MJ, Hoover-Regan ML (2014) Pediatric clinical trials: a US perspective. *Open J Clin Trials*6: 127-138.
8. Oberle K, Singhal N, Huber J, Burgess E (2000) Development of an instrument to investigate parents' perceptions of research with newborn babies. *Nurs Ethics* 7: 327-338.[Crossref]
9. Singhal N1, Oberle K, Burgess E, Huber-Okrainec J (2002) Parents' perceptions of research with newborns. *J Perinatol*22: 57-63.[Crossref]
10. Nabulsi M, Khalil Y, Makhoul J (2011) Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective. *J Med Ethics*37:420-423. [Crossref]
11. Nasef N, Shabaan A, Mohammed S, Kandel S, Settin A, et al. (2014) Factors influencing parental consent for participation in clinical research involving their children in Egypt. *East Mediterr Health J*20:162-168. [Crossref]
12. Hoberman A, Shaikh N, Bhatnagar S, Haralam MA, Kearney DH, et al. (2013) Factors that influence parental decisions to participate in clinical research: consenters vsnonconsenters. JAMA Pediatr167:561-566. [Crossref]
13. Wilman E, Megone C, Oliver S, Duley L, Gyte G, et al. (2015) The ethical issues regarding consent to clinical trials with pre-term or sick neonates: a systematic review (framework synthesis) of the empirical research. Trials 16:502. [Crossref]
14. Woolfall K, Shilling V, Hickey H, Smyth RL, Sowden E, et al. (2013) Parents' agendas in paediatric clinical trial recruitment are different from researchers' and often remain unvoiced: a qualitative study. PLoS One 8:e67352. [Crossref]
15. Byrne-Davis LM, Salmon P, Gravenhorst K, Eden TO, Young B (2010) Balancing high accrual and ethical recruitment in paediatric oncology: a qualitative study of the 'look and feel' of clinical trial discussions. BMC Med Res Methodol10:101. [Crossref]
16. Hoehn KS, Nathan A, White LE, Ittenbach RF, Reynolds WW, et al. (2009) Parental perception of time and decision-making in neonatal research. *J Perinatol*29: 508-511. [Crossref]