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ABSTRACT

Background Paediatric clinical research faces unique challenges that compromise optimal recruitment of children into clinical trials. A main barrier to enrolment of children is parental misconceptions about the research process. In developing countries, there is a knowledge gap regarding parental perceptions of and attitudes towards their children's participation in clinical trials.

Objective To explore such perceptions and attitudes in Lebanese parents.

Study design 33 in-depth interviews were conducted with parents with and without previous research experience. Interviews were tape-recorded, transcribed in colloquial Arabic, and later subjected to thematic analysis.

Results Benefit/risk ratio assessment was a major determinant of parental consent. 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, a complex informed consent form and misunderstanding of the term 'randomisation' hindered parental approval of participation.

Conclusion Lebanese parents have perceptions of and attitudes towards children's participation in clinical trials that are similar to those reported from the industrialised world. Improving communication with parents and building trust between researchers and parents is important for successful recruitment. Investigators planning to conduct paediatric trials in developing countries need to simplify consent forms and devise new ways to explain randomisation.

INTRODUCTION

Paediatric clinical research faces unique ethical and practical challenges. One main obstacle is the fact that children are unable to give full informed consent and thus have to rely on their parents to make decisions on their behalf. Parents, on the other hand, feel the obligation to protect their children from potential harm and may refuse to enrol their children in clinical trials. Consequently, the medical literature suffers from a relative paucity of good-quality paediatric trials.[1 2] Whereas publication of adult randomised clinical trials (RCTs) increased by 4.71/year between 1985 and 2004, publication of paediatric RCTs increased by 0.4/year.[2] In one study of community paediatric practice, only 40% of clinical decisions involving children were found to be evidence-based or supported by good-quality trials.[3] Moreover, most paediatric studies were found to suffer from small sample sizes, which make them less likely to detect important treatment effects.[1]

Barriers to children's recruitment into clinical trials may be due to parental misconceptions about the research process such as the use of placebo, the meaning of randomisation, and perceived risks of research.[4–8] Thus, it is essential for researchers to understand parental fears, concerns and preconceived ideas about clinical research. Although studies exploring parental experiences in paediatric trials have been conducted in Western countries, we found no studies investigating similar parental experiences from non-industrialised countries, where clinical research faces economic, cultural and practical obstacles.[9 10] This qualitative study is the first one, to our knowledge, to explore the attitudes of parents from a developing country towards child participation in research trials. The findings of this study may identify recruitment barriers, and provide insight for researchers designing recruitment strategies for trials in developing countries.

METHODS

We adopted a qualitative research approach, which assumes that 'reality is subjective and multiple, as seen or experienced by individuals participating in a study'.[11] Qualitative research is 'descriptive' of the process and the meanings gained through words, and is 'inductive' in the sense that the researcher builds 'abstractions, concepts, hypothesis and theories from details'.[11] Qualitative research methods are therefore better than quantitative ones in capturing the feelings and perceptions of individuals, or understanding their attitudes and experiences. As our study aimed to explore parental feelings about their children's enrolment in clinical trials, parental understanding of informed consent and randomisation, and their perception of harms and benefits of clinical research, qualitative methods were best suited.

Between February and May 2009, we conducted 33 in-depth interviews with parents presenting to the American University of Beirut Medical Center (AUBMC) in Lebanon. In the first of two phases, we interviewed 13 parents whose children were enrolled in a vaccine clinical trial conducted at AUBMC during the summer of 2008. The aim of the trial was to compare serum antibody responses to two types of meningococcal vaccine administered as injections in 2–20-year-old subjects. We used an interview schedule composed of five open-ended questions (see appendix I online only) to explore their feelings about, perceptions of and attitudes towards paediatric clinical research in

view of previous experience. In the second phase, 20 parents with no experience of clinical research were enrolled: 11 were interviewed on the paediatric ward where their children were inpatients, and nine in paediatric private clinics. Parents were presented with a hypothetical scenario of a clinical trial comparing the effectiveness of alternating oral antipyretics versus monotherapy in 1–13-year-old children. Parents were asked whether they would approve their children's enrolment in that trial. An interview guide of six open-ended questions was used in light of the themes generated from analysing phase 1 interviews (see appendix II online only).

Tape-recorded interviews were transcribed in colloquial Arabic and submitted to thematic analysis. Recurrent themes and sentences emerging from raw data were identified and summarised on spreadsheets for data management. Subsequently, minor and major themes were generated to provide insight into parental perceptions and attitudes. The study was stopped when saturation of themes was felt to be reached by the 33rd interview.

ETHICAL CONSIDERATIONS

This study was approved by the institutional review board at AUBMC. A research assistant trained in qualitative research methods invited parents to participate in the study, explained study objectives and procedures, read the informed consent form to the parent, and obtained written consent for tape-recorded interviews. Participants were assured of confidentiality and anonymity of interview recordings and transcripts, as well as of behaviours observed any time during the study. Parents were also assured that participation and withdrawal from the study were voluntary and would not affect the care provided to their children, and that information gathered would be used solely for the purpose of the study.

FINDINGS

The themes generated from analysis of interviews of both phases of the study were quite similar, suggesting that perceptions and attitudes of parents who were new to research experience are not much different from those with previous research experience. Hence we decided to combine the findings of the two groups and summarise similar themes under the same headings.

Fear

A main barrier to parental consent to children's enrolment in clinical trials was parental fear of possible harm to their children from the study and fear of associated painful procedures. Fear of potential short-term or long-term adverse events was put forward by 16 participants and is reflected in the following quotes:

> I was afraid that the vaccine could cause the disease itself instead of resulting in immunity, or that there may be not enough research about it! [Mother and nurse]

> The fear is that some weird side effect could happen to her that happens to one in every 10 million kids…let's say it happens to her…I'll never forgive myself…I agree that things need to be tried out but I'm a mother, I'm selfish, I don't want it to be on my child! [Mother of an only child]

Although most parents declared that they would allow their children to undergo a necessary painful procedure such as blood testing, five expressed their discomfort with testing, describing it as a 'bad experience'. Parents felt that researchers should hire experienced personnel to perform such procedures.

> …the kids suffered a lot at the time! Now, for example, it will be a problem if they have to undergo blood testing in the future, they worry a lot!! [Mother of three]

> …I didn't want to bother the doctor, I just wanted to ask her if I could take the kids to the lab to do the blood test or if they could ask an expert to take blood from children! [Father and hospital employee]

Parental fear was heightened because of the monetary issues involved: the vaccine was provided for free while in reality it is expensive; transportation expenses were compensated and this is also unfamiliar to them.

> My fears are for later and not now! Is it possible that it may affect her in any way later? When she is older? Especially that I am not paying for it! [Mother of an only child]

> …so all parents will be scared, especially because the vaccine is provided for free when we know it is expensive! When we come here, they give us money for our transportation! This is scary you know!! [Mother of four]

Randomisation

Of the 20 parents approached about participation in the hypothetical clinical trial, only six consented. The concepts of consent and randomisation were the issues most pointed out by parents, especially those who came from a lower social position, or those whose educational background did not expose them to research concepts. These parents struggled with the term 'randomisation' and its purpose, despite interviewers' lengthy attempts to explain it. Four interviewees refused to enrol their children in studies that randomise subjects, as they considered it is marked with uncertainty and anxiety, especially that the parent has no control over what intervention the child was receiving:

> Neither me nor you even! So we don't know what's happening! Did my child take the vaccine or did he take the placebo? How can I be reassured? [Mother and nurse]

The Arabic translation for the word 'randomisation' is 'ashwa'I' meaning happening in a haphazard way. There is no other Arabic equivalent. Parental anxiety about this process, understood as 'going into the unknown' is therefore understandable. Similar findings of parental misunderstanding of randomisation and concern about lack of control over children's treatments were also reported by Caldwell *et al*[12] and Wiley *et al*[13] among parents of children with cancer.

In contrast, parents visiting private clinics, who belong to middle and high socioeconomic classes, seemed to have a better understanding of randomisation and understood the English term. For them, it was an appropriate or 'fair' method of conducting research, of which they approved. Six mothers expressed their consent to randomisation in any clinical trial involving their children.

> It's a computer selection, definitely it's random. It's much better…the results will be more reliable and valid…If I accept the study, I would accept either/or situation…[Mother of two]

> I'll be comfortable knowing that my child was assigned to this treatment randomly and not because of a special consideration…I think it is fair…it's better that way…[Another mother of two]

Informed consent

It is worth noting that only four parents from the vaccine study remembered the consent process and that it was voluntary.

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Many of the participants found the form difficult because of the complex medical terminology and its length, which required time to read and comprehend and was therefore a source of anxiety for them. Parents required the opinion of other trusted people, such as their husband, their paediatrician or a lawyer, before signing it.

> …this sentence scares me… you should not put it…just mention that there may be side effects…ok…but doing a urine test to make sure? it's scary. Just mention it orally, no need for papers![Mother of a hospitalised baby]

> …you see…it had many pages…you cannot read it all during the interview…you need to take it home and read it at night when it is calm and the kids are not around you…you need to read it carefully and thoroughly because the words…medical words…I'm not a doctor, and I need to ask about these words…I need to ask my paediatrician, then take a week to think…I should understand each word before I say okay and sign.[Mother who was sceptical about the vaccine administered to her two daughters]

Although most parents considered the consent form to be necessary, one may argue that seeking a written rather than an oral consent may have contributed to their anxiety. In Arab contexts such as these, signatures are not required except for formal transactions, such as buying or selling property, or changes in personal status, and these are binding.

Benefits

Among the factors that facilitated recruitment of children into clinical trials were the perceived benefits, either to the child, which was a recurring theme in all 13 interviews with parents with previous research experience, or benefits to other children.

> …after all, it is something that benefited my boy, you know…it is the meningitis vaccine! I agreed because it offers protection for my child…[Mother of two]

> I support research, and if it is for children, then OK, provided children will benefit and there are no side effects or problems… [Mother of a newborn]

> I was just telling my husband that I will do anything that will help my child get better…fever is a very important issue for me personally…[Mother of a hospitalised boy]

> It is beneficial for science because many children suffer from fever. If everyone refuses to participate, how can there be trials for science to improve?[Mother of two]

Even though parents mentioned benefit to science as a reason to participate, benefit to the child was the parents' priority. If a parent were convinced that the research subject would result in direct benefit to the child, and that harms were mild or minimal, then he/she would be more likely to consent. This finding is consistent with previous studies revealing parental balance of risks and benefits to play a major role in their decision about their children's participation in clinical trials.[7 12 14]

While monetary issues were a barrier to participation for some parents, four parents revealed that they participated in research for financial gains. These consented to participate in the vaccine study because it was provided for free. Their financial problems led them to gratefully participate.

> Our financial situation is hard, so we said since the vaccine is expensive, then ok!![Mother who was sceptical about the vaccine administered to her two daughters]

> You know, frankly…they are helping parents save on many things…this vaccine I believe is expensive, and they gave it to us free,…I should be the one to thank them and not vice versa!! [Mother of three]

Trust

Trust in the doctor and in the institution where the study is conducted was mentioned by 14 parents and seemed to play a main role in facilitating or hindering participation. The medical doctor is a crucial figure in their narratives. The doctor, in this case the paediatrician, is consulted about the consent form, and, when the study received approval from the physician, this facilitated parents' consent.

> our paediatrician advised us to take the study vaccine since it is better than the one she was going to give my child any way, then why not try?[Mother of two]

> …if my doctor tells me I can participate in this research, then yes I will do that… Father and hospital employee]

> Yes. I asked my paediatrician about the doctor responsible for the study and whether I can vaccinate my children. She reassured me and encouraged me to participate. Mother of four]

In other cases, five mothers wanted their doctors to assign their children to the intervention rather than a computerised randomisation, which they felt was a lifeless risky way of treating a child.

> …a person is always hesitant… he needs to be sure. If my doctor chooses, you know… it's not like the computer. No. I prefer that my doctor chooses the treatment…[Mother of a hospitalised baby boy]

However, despite the parents' trust in their physician, the parents would decline if they felt pressured to consent. This appeared in the narratives of educated parents who seemed empowered to make decisions on their own by virtue of their experiences and educational backgrounds.

> If I trust him and he has been my doctor for a long time: yes…if I feel he just wants his study to proceed and I'm not very sure: no! Well-to-do mother attending private clinic]

The mistrust in doctors stems from fear of medical errors, especially voiced by two parents who had such experiences before.

> The thing that scares me most is doctor's mistakes! My older son died in a hospital. It could have been avoided. This is why I am wary! Another mother who lost a child]

> I do not put myself in the unknown! It's not a game at all! [Mother of a boy with fever]

At a higher level, trust in the institution conducting the study was also a decisive factor in parents' participation. This trust stemmed from the credibility that a university has in the eyes of parents, which seemed to minimise parents' fears, as they believed that the institution would not risk putting its good reputation at stake.

> …the fact that you are coming to this university and to a doctor from this university means that you should not be afraid from anything!![Mother of two]

> I said to my husband: what if the vaccine harmed our boy? He said that he doesn't think so because the University will not conduct a study that will cause harm to any child, even if it is one in million children![Another mother of two]

Having a previous positive experience with research encourages further participation, whereas lack of such experience or lack of trust in research was a strong barrier.

> I believe that they will be encouraged once they find that their first experience was safe[Hospital employee father]

> I don't want my child to participate…I don't want him to try even a drop of water if it is for research…[A mother who lost a child]

Despite their understanding of the research process, one could argue that parents with higher socioeconomic backgrounds were more critical, less likely to blindly trust physicians, and more difficult to recruit.

Other barriers

Other issues that came up less frequently in the interviews relate to additional time and effort that is required of parents involved in trials

> I don't want to worry about such things…I don't have time for it! [A working mother]

Parents' advice to researchers about what needs to be done to ensure successful recruitment of children in clinical trials included holding simple information sessions or lectures with parents to explain all study details, allowing interaction among parents, and thinking out loud to reassure parents, something they desperately wanted to hear from the researchers.

CONCLUSIONS AND IMPLICATIONS FOR PRACTICE

This qualitative study, the first to explore parental perceptions of and attitudes towards paediatric trials in a developing country, reveals findings similar to those reported from the industrialised world.[15] Whereas parental fears of harm were a strong barrier, trust in physicians facilitated parental approval of children's participation in trials.[15] Consequently, investigators need to invest in this trust by designing recruitment strategies that alleviate parental fears and anxiety, improving communication with parents through conferences dedicated to detailed study explanation,[16] and establishing collaborations with community physicians who are recognised by their clients as trusted sources of information and advice and who may facilitate the recruitment process. Informed consent forms should be simple, easy to understand by lay people, and free from complex medical terminology. Parents need to be given enough time to comprehend the consent form and to consult their primary physicians.

Parental assessment of benefit/risk ratio is a major determinant of their consent. Hence, investigators need to highlight the direct benefit to the child, assuring parents that their understanding of risks is realistic and not inflated. When painful procedures are involved, it is vital that both parent and child understand the relevance of such procedures, the knowledge gained, and the potential benefit to the child. Needless to say, appropriate measures for minimising pain should be instituted, such as using local anaesthetic or hiring experienced specialists to perform procedures. Moreover, investigators should devise new ways to explain randomisation to enhance parental understanding and children's enrolment. Special attention should be paid to 'vulnerable' parents who may consent for financial reasons or because of blind trust in physicians or confusion between 'research' and 'service'.

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Competing interests None.

Patient consent Obtained.

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