REVIEW

Consent for neonatal research

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Arch Dis Child Fetal Neonatal Ed 2006;91:F374–F376. doi: 10.1136/adc.2005.075036

Inherent to all medical research is respect for the rights of the individual. Neonatal research is made more complex by the issue of proxy consent. Obtaining valid informed consent for entry of an infant into a research project needs to deal with this complexity. New evidence on the role and responsibilities of parents in giving consent has implications for all clinical staff that are considering embarking on and/or recruiting infants in research projects. This review explores the issues around informed consent for neonatal research and provides a framework by which consent could be improved. It is to be hoped that such improvements to the process will increase recruitment of infants to research studies while enhancing the validity of the consent process.

- The consent should be given freely and voluntarily.
- Sufficient information should be given to make an informed choice.⁴
- The understanding of the subject is sufficient to make an informed choice.
- The person giving consent must be mentally competent.⁵

When these four principles are applied to neonatal research, the issues become more complicated because of proxy consent. Examining each of the factors that make consent valid gives a greater understanding of the issues.

Voluntariness

Assessing the voluntariness of parents giving consent has been limited to only a few studies. In the Euricon study, the group showed that only 10% of parents appeared to have problems with the voluntariness of their consent, whereas 55% of neonatologists had concerns on behalf of the parents, in this area.⁶ Factors raised included the pressure of time, the moral obligation parents had towards the clinicians, neonatal unit, or society, and the tendency of desperate parents to try anything.⁷ It has been suggested that less educated parents or those from lower socio-economic groups are more likely to give consent. This has been questioned in other studies.^{8,9} Our view is that there is no convincing evidence to show that socioeconomic status consistently influences the consent process.⁶

Information and understanding

Parental understanding of information given about a trial has been shown to be limited.¹⁰ Recruitment to urgent trials is higher than for non-urgent, and it has been suggested that this is a result of poor understanding; hence the validity of the consent must be questioned.¹¹

Information sheets are seen by ethics committees as extremely important to information and understanding, but parents often found them too difficult to understand. In fact, they were more likely to rely on the information provided by the person obtaining consent in making their decision.

Competence

The Griffiths report suggested that, under the stressful conditions in which parents find themselves, consent can never be certain to be valid.¹² Forty per cent of parents have been shown to be not competent when approached for consent because they were emotionally overwhelmed, preoccupied with their baby, or unwell following labour. To highlight this stress for parents, nearly 20% of parents did not remember (or were

Since 1947 the Nuremburg Code has underpinned the ethics of medical research. The code states that consent must be voluntary, that there must be freedom of choice, and the participant must have sufficient understanding of the subject matter.¹ These components remain at the heart of the consent process. In 1964, The Declaration of Helsinki (updated several times subsequently) further emphasised the requirement for the needs of the individual to override those of science and society.² It is with these two major ethical codes in mind that we approach the subject of consent in neonatal research today. In the past five years, there has been an increasing body of research examining parents' experience of the consent process that provides a framework for improvement. We here review the current literature and make recommendations for improvements to the consent process.

In general neonatal research trials fall into three categories:

- Emergency; treatment must be immediate
- Urgent; trials aimed at potentially life saving interventions although some time is available before entry—for example, TOBY and ECMO
- Non-urgent; time to obtain consent may be many days, such as for feeding trials

Each trial type will influence the validity of the consent process.

VALIDITY

The over-riding principle of the consent process for biomedical research is respect for autonomy.³ The components needed to make the consent process valid are as follows.

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Accepted
15 December 2005

Key points

For consent to neonatal research to be valid it must be

- Voluntary
- Understood
- Given by a competent person
- Given by the legal guardian

unsure) whether they had consented to their child entering the study 18 months after enrolment.¹³

ETHICAL AND LEGAL ISSUES

The apparent opposing positions on the influence of socio-economic status highlights the need to assess the autonomy of parents. The way in which information is given needs to take into account parental abilities.

It has been shown that parents are often unaware of the involvement and role of the ethics committee. Armed with this knowledge, parents said that they would feel less burdened. However, some commentators are concerned that provision of information on the ethics committee may be seen as coercion. Those parents who were aware of the role of the ethics committee clearly stated that they still wanted to be asked for consent.¹⁴

Awareness that parents can withdraw from a trial is a key component to a valid consent process. However, two studies have reported that only about 70% of parents understood this.^{7,9}

PARENTAL VIEWS

Recent studies have explored the views of parents on the consent process. One report suggested that 32% of parents would prefer the doctor to decide on trial entry,⁸ but many subsequent reports disagree, with up to 98% of parents wanting to make the decision.^{6,9,15} In fact, many strongly believe that it is their right to do so. Despite clinicians' concern that parents should be spared the additional stress, studies show that parents did not feel pressured to give consent^{9,16} and the majority remained happy with their decision.

There are three prime motivators for parents to consent to trial entry.

- Improved care of future babies. This altruistic motivator ranges from 48% to 94% depending on the type of research study.^{6,15,16}
- Direct personal benefit.^{11,16} Many feel entering a trial will get their baby treatment that is better than the standard treatment.¹⁴ It could be argued this is because of a lack of understanding of randomisation, but perhaps it is merely a natural human reaction.
- Neutrality.¹⁶ Parents see no harm attached to the study so why not give consent? Again, this may be a fault in understanding; most treatments have risk associated with them. The high regard in which doctors may be held could play a part in this, with parents trusting in the clinicians fully.

Studies into parental reasons for refusal of consent are limited but factors highlighted are:

- The risks of the trial are too great
- An inherent anti-experimentation belief¹⁶
- Clinicians' approach to parents⁶

The time that parents have to decide on trial entry has been suggested to be too short as the prime reason for less than valid consent.^{11,14} However, when asked, parents are generally happy with the time they have, regardless of the type of study⁹ (emergency, urgent, or non-urgent). Timing of the request is a more common concern.¹⁶ There are reports of parents being woken from sleep for consent or being asked half an hour before surgery.

The request for consent may add stress to an already stressful situation.⁹ However, parents that concur with this are in the minority (26–38%).

In the past it was felt that parents would not consent to more than one trial at a time. However, Morley *et al*¹⁵ showed 74% of parents would be happy to join two or more studies. In a model proposed for obtaining informed consent, Golec *et al*¹⁷ suggest that, if a parent is to be approached for more than one study, these requests should be made at least 48 hours apart. However, evidence to support this is lacking.

Many parents have difficulty with many of the concepts and language used in research studies.⁵ The concept of randomisation is an example: if randomised to receive standard treatment, parents may feel that their infant is missing out on a potentially beneficial treatment.¹⁰ The position of equipoise by doctors, inherent in all randomised trials, is difficult for parents to understand as they usually experience positive treatment decisions. There is a danger that parents lose trust in the healthcare providers.

IMPROVEMENTS TO THE CONSENT PROCESS

Clearly, the consent process can always be improved. The simplest adjustments that can be made that have been shown to have a positive effect on recruitment are those of timing and the environment in which the request is made. By simply thinking about these two basic points, the process is already improved. A knowledge of parental views on agreeing, or not, to research will also help.

Antenatal consent has been popular with parents,^{15,16} despite the fact that it may burden them with unnecessary information.¹⁷ Validity of consent obtained during labour must be questionable. Equally, obtaining consent from high risk pregnancies may put undue stress on parents.¹⁸ As the fetus has no legal rights, antenatal consent raises legal questions.

Some commentators advocate informing prospective parents that research trials are undertaken in the hospital of delivery. They suggest an "opt out" clause if they do not want to participate. It has been suggested that this may decrease parental stress and increase recruitment.¹⁹ This may be a step too far, but providing information in the antenatal period may be appropriate.

Key points

Parents

- want to be involved in the decision to enter a research project even those who felt significant added stress by the research project
- agree to consent for societal benefit, personal gain, and the perception of no harm
- refuse consent because of the risk of harm, anti-experimentation beliefs, or clinician approach
- would agree to their baby being in more than one trial
- find some of the concepts of trials difficult to understand
- rely on verbal explanation and information sheets in making decisions

Key points

Consent may be improved by

- Antenatal awareness and discussion
- Clear and well regulated information
- Training of those asking for consent
- Continuing two way communication

The American regulatory bodies have developed a Code for Exemption from Informed Consent Requirements for Emergency Research. This involves the trial being begun before consent is obtained but gaining it at the earliest opportunity. Wiswell²⁰ and the Resair-2 study²¹ have used this approach in neonatal research.

Allmark and Mason have studied the outcome of a continuing process for obtaining consent as part of the TOBY (body cooling) trial. Early results (P Allmark and S Mason, personal communication) indicate that this standardised continuing consent process improved consent validity. Parents are reported as finding the process helpful, especially the follow up consultations that occurred after signed consent, alongside but separate from daily updates on clinical progress. Full details will hopefully be available soon. If this continuing process of consent is in fact proven, it will provide a new framework for the way in which consent is handled in the future.

Presumed consent assumes the scientific robustness of the research and the welfare of the participant by other measures. Parents do not like this concept.⁶ The findings are similar when Zelen randomisation is suggested (whereby consent is requested after randomisation only of the participants in the treatment arm; other participants receive standard treatment and so are not required to give consent).²²

CLINICIANS' ROLE IN CONSENT

The Euricon trial was the only study we could find that specifically looked at the clinicians' involvement in the consent process. This showed that most doctors asking for consent had received no training in the process, although many were obtaining consent appropriately. We contend that this is unacceptable and that any clinician involved in obtaining consent must have appropriate training.

Although this paper focuses on consent for research, the principles are applicable to consent to treatment. The British Association of Perinatal Medicine framework for good practice²³ highlights two key points of two way communication and documentation. This is just as critical in consent for neonatal research. Documentation should be meticulous and where possible witnessed. Clear communication with the parents will always improve trust and help avoid potential disputes.

CONCLUSION

Improvements to the consent process are essential to meet research governance rules and parents' rights as legal guardians. It is to be hoped improvements to the consent process will improve recruitment rates to neonatal trials. All clinicians involved in neonatal research should fully

understand the principles of consent and more importantly the increasing body of literature around parents' experiences in being approached and giving consent.

ACKNOWLEDGEMENTS

We thank Peter Allmark and Su Mason for their information regarding the continuous consent process.

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Competing interests: none declared

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