Nurses’ role in platelet transfusion clinical trials

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Abstract

This article describes the crucial role of research nurses in studies coordinated by the NHS Blood and Transplant Clinical Trials Unit (CTU), using two recent trials studying platelet transfusions in adults and neonates as examples. CTU studies are coordinated by trial managers, most of whom are or were registered nurses, which supports relationships with research nurses in participating hospitals. During trials the CTU sustains research nurses with ongoing education and training, and establishes cooperative working between nurses and the unit, and between nurses in different locations. Regular feedback from research nurses guides the design and management of clinical trials.

NHS Blood and Transplant (NHSBT) is principally recognised for its work in blood donation and organ donation and transplantation, although its mission is much broader. The organisation is a special health authority that provides blood components and coordinating organ donation for the NHS.

It also conducts world-class research in the fields of transfusion medicine, organ donation, tissues and stem cells. Its mission is to save and improve lives through the many services it offers. The NHSBT Research and Development Department (R&D) runs an overarching programme consisting of two streams:
» Researching and delivering new technology and innovations;
» Generating evidence through clinical trials to inform national safety policies and clinical guidelines, primarily in the fields of transfusion medicine, organ donation and transplantation, tissue and stem cell therapy.

The NHSBT Clinical Trials Unit (CTU) supports these trials and has completed many observational studies and large randomised controlled trials (RCTs) in the field of transfusion medicine. These focus on the safe and effective use of blood components. Results from these studies are now influencing clinical practice.

Whether working directly with patients and participants, or in the CTU as trial, project and senior managers, research nurses play a crucial part in CTU trials. This article illustrates nursing contributions using two studies on the clinical use of platelet transfusions (Boxes 1 and 2).

The TOPPS trial
The aim of the TOPPS trial was to find out whether it was as safe to give platelets only when patients with thrombocytopenia needed them (when bleeding) as the standard, recommended clinical practice of transfusing platelets prophylactically (to prevent bleeding) when the platelet count was ≤10 x 10⁹/l (compared with normal values of 150–400 x 10⁹/l).

Patients with haematological malignancies were recruited from adult haematology wards in eight UK and three Australian hospitals. They were randomised either to receive prophylactic transfusions or to receive platelet transfusions only when needed for bleeding. The study’s findings were published in 2008.

The PlaNeT-2 trial
The PlaNeT-2 trial (Platelet transfusions in Neonates: Transfusion or No Transfusion?) was a randomised controlled trial to determine whether it was as safe to give platelets prophylactically to neonates with neonatal alloimmune thrombocytopenia (NAIT) and a low platelet count as the standard care of administering platelet transfusions only when the platelet count fell below a specific level. The study was completed in 2014 and the findings were published in 2015.

Recent and current trials in platelet transfusion are influencing clinical practice and breaking new ground

Registered nurses in the CTU have a cooperative relationship with research nurses at hospital sites

Nurses are key to platelet therapy trials
after documented signs and symptoms of bleeding. A total of 600 patients were recruited over five years, 300 in each group. Information about participants’ bleeding and platelet counts was collected daily. The results showed that clinically significant bleeding occurred in 50% of patients in the therapeutic (non-prophylactic) group compared with 43% patients receiving prophylactic transfusions.

The study did not show that a non-prophylactic strategy for platelet transfusions was as good as (or non-inferior to) a prophylactic strategy in relation to the frequency of bleeding. The results therefore supported the continued use of prophylactic platelets in patients with thrombocytopenia.

However, the high level of bleeding in both trial groups suggests that current policies for prophylactic platelet transfusion have a limited role in reducing much of the bleeding in haematology patients undergoing intensive chemotherapy and/or stem cell transplantation and that there is a need for new treatment strategies to support this patient group.

As a result, we are preparing a new RCT: TREATT (Trial to Evaluate Tranexamic acid therapy in thrombocytopenia) to study patients given anti-fibrinolytic tranexamic acid prophylactically, compared with placebo, as an adjunct to platelet transfusion.

The trial management for TOPPS was led by research nurses, which contributed to its success. Nurses in the CTU understand the realities of life on haematology wards and appreciate the difficulties of approaching patients to enter the trial, or collecting data on a daily basis. These are some of the key activities nurses were involved in during the TOPPS trial.

**Screening**

Screening for possible participants for TOPPS involved research nurses reviewing inpatients and outpatients in their respective units; checking treatment lists; and coordinating with the local clinical nurse specialists, outpatient department clinic, day unit teams and haematology clinicians. This can involve investigating a large number of potential participants, which can be very time-consuming.

**Consenting**

The consent process was coordinated by research nurses. They approached patients to discuss the workings of the trial, explaining any possible benefits or risks; ensuring they were fully informed, including having the opportunity to ask questions; and giving them time to think about what would be involved and discuss with friends and family, before providing a signed consent to participate in the trial. Traditionally consenting has been seen as a task only undertaken by doctors, but it is increasingly carried out by appropriately trained nurses.

**Data collection**

All trials require information to be collected from the participants in case report forms (CRFs) to answer the trial question and ensure the safety of participants. A crucial component of the TOPPS data collection was the accurate and consistent assessment of bleeding observed in participants. In the past this has been subjective, so one clinician’s “mild” or “insignificant” bleeding could easily be another’s “moderate” and “of clinical concern”. It was necessary to ensure that all investigators at the 14 participating hospitals were assessing and recording patients’ bleeding in the same way.

A nurse-led project group was established to investigate different methods of assessing bleeding and to design a form to record this for the trial. This group also concluded that patient self-assessment was valuable and particularly useful after discharge from hospital (Dyer et al, 2006; Stanworth et al, 2006).

The aim of the bleeding assessment form was to ensure objective and consistent measurements were recorded every day, achieving not only consistency between the different research nurses and registrars at each haematology unit, but also between the different hospitals involved. While inpatient assessment was undertaken every day, after discharge participants were given a “bleeding diary” to complete daily at home until the end of the study at day 30, and a comprehensive self-assessment form to complete if they observed any bleeding.

This form was similar to the clinical bleeding assessment, but written in plain English rather than technical medical terms. The paperwork was collected by the research nurses at outpatient clinics or returned by post.

**Training and sharing information**

Good communication between research nurses and CTU staff is fundamental, so while the trial was running we held six-monthly meetings for the nurses. These were an opportunity for training and trial updates, but also for site nurses to share problems and successes with the CTU and with each other. Regular feedback between the trial team and research nurses guided trial management.

The trial manager – a research nurse herself – sent out a monthly newsletter to pass on new developments, and respond to comments and observations from hospital research nurses.

**Communicating**

Many patients move between hospitals – for example, going to a large tertiary centre for treatment such as a stem cell transplant, but returning to their local hospital for outpatient follow-up. Research nurses at trial sites needed to liaise with the haematology teams, including the clinical nurse specialists, at nearby hospitals to keep up with what was happening to their TOPPS patients.
PlaNeT-2
PlaNeT-2 is a neonatal study to compare two different thresholds for platelet transfusions to determine the safest level at which to prophylactically transfuse preterm babies with severe thrombocytopenia. It is the first RCT to focus on neonatal platelets and thrombocytopenia – there has been little clinical research on neonatal transfusion medicine. Clinical practice in this area is largely based on anecdote and clinicians’ “gut instincts”.

More than 40 centres in the UK and the Netherlands are taking part in PlaNeT-2, and at least one research nurse is involved at nearly every centre. The co-ordinating team rely on the support of these nurses for the success of the trial. Research nurses involvement in PlaNeT-2 covers some of these areas outlined below:

Screening
Babies suitable for inclusion in PlaNeT-2 are rare – a large neonatal intensive care unit (NICU) will only recruit one a month. So the trial cannot afford to miss any eligible babies and PlaNeT-2 research nurses have to be alert to changes in babies’ condition that may allow them to enter the trial.

Only a third of the babies consented go on to be randomised because, although they may meet the initial inclusion criteria, they may fail at subsequent hurdles. Parents can give informed consent at a platelet level below 100 x 10^9/l (the normal range for a newborn baby is 150–350 x 10^9/l), but babies can only be randomised if they become severely thrombocytopenic (<50 x 10^9/l).

The window of opportunity to randomise a baby can be extremely small. All the research nurses have a system of reviewing platelet counts daily, and often have back-up plans for when they are not on the unit. This requires good co-ordination and planning with the local team.

Consenting
Gaining informed consent from parents or guardians for their baby to be recruited to PlaNeT-2 brings challenges. These babies are very ill and their parents are under stress. The trial can be difficult for people with no medical background to understand, so those seeking informed consent must be excellent communicators.

While only doctors seek consent in some sites, in others the research nurses perform this function, and frequently their consent rate is higher than that of the doctors. The nurses are usually more accessible to parents and may have developed a good relationship with them.

Often parents have been approached to participate in several research trials before their baby is eligible for PlaNeT-2, so research staff can be reluctant to approach them again. However, research has shown that parents in neonatal units prefer to be approached for studies, so they can make up their own mind, than not be approached because of the paternalistic attitudes of health professionals (Morley et al, 2005).

The PlaNeT-2 research nurses must tread a fine line between empathy and compassion, and allowing parents to be involved in research if they wish.

Communicating
PlaNeT-2 babies are often transferred to different units – for example, because of pressure on intensive care cots, they may be sent to another hospital when they have stabilised, and families also often prefer to have their baby at a centre nearer to their home. We have developed a network of neonatal nurses who cover much of the UK. There is a central coordinating project team in Cambridge, but much of the work to obtain data or pass on relevant information is performed by the research nurses who link up across the country.

For the trial it is necessary to obtain two-year follow-up data from neuro-developmental assessments, and the local research nurses are responsible for collecting this. Some of the nurses visit follow-up clinics and stay in touch with parents, which makes it easier for them to do this.

Data collection
Once a baby is randomised, it is often the research nurses who complete the data collection forms and keep the trial on track. Data from each baby is valuable to us and we owe it to the parents to ensure their contribution is worthwhile. We are lucky that most PlaNeT-2 research nurses are specialists in neonatal medicine because the data we require is detailed and a high level of knowledge is needed.

Training and sharing information
Because eligible babies are so rare, it is important to keep PlaNeT-2 in the minds of everyone involved. The research nurses often run training updates for new staff and have developed much of the material that is used. This is then shared among the group via a website (www.planet-2.com), where it can be uploaded and accessed by anyone in the trial. A series of presentations created by one research nurse has been used for study days and refresher training, and she has now been co-opted to our trial management group so we can represent the research nurse perspective of the trial.

We publish a newsletter four times a year to which the research nurses contribute articles about the trial and on courses or subjects that will be of interest to the rest of the group, either for PlaNeT-2 or for their research interests generally.

Conclusion
The NHSBT Clinical Trials Unit is a multidisciplinary group that includes nurses, doctors, trial and data managers, statisticians and administrative support staff.

Many senior staff are or were registered nurses and this supports our collaboration with hospital-based research nurses. We understand the situations and environments our colleagues work in, and aim to offer them the best support possible.

We also benefit greatly from the two-way flow of information: feedback from hospital research nurses has contributed in many ways to trial design, including the writing of trial protocols, format of the data collection forms, and training and education material. This is demonstrated in the trials discussed in this article, but also applies to other CTU studies.

References