Effect of elective blood transfusion on cerebral, hepatic and muscle regional oxygenation and cardiorespiratory stability in neonates

Study type: Prospective observational single-centre study

Objectives:
The primary aim of this study is to determine whether elective blood transfusion to treat anaemia in neonates improves cerebral, hepatic and muscle regional oxygenation at the time of transfusion.

The secondary aims of this study include whether:
1. Elective blood transfusion to treat anaemia in neonates results in a sustained improvement in cerebral and somatic oxygenation at 1 and 5 days after transfusion
2. Elective blood transfusion to treat anaemia in neonates results in improvement in cardiorespiratory stability defined as a reduction in the frequency and duration of desaturation (peripheral arterial saturation) and bradycardia.

Inclusion and exclusion criteria:

Infants will be considered for recruitment into the study if the clinical team in Wellington NICU makes a decision to give non-urgent blood transfusion to inpatients in Wellington NICU.

Patients with following criteria will be excluded from the study if:
- Urgent blood transfusion is required
- Mechanically ventilated at the time of transfusion
- Undergoing treatment for systemic infection with broad spectrum antibiotics
- Receiving medical treatment or are awaiting surgery for a haemodynamically significant patent ductus arteriosus (PDA)
- Significantly oedematous

Study methods:
This is an observational study, and as such the decision to give a blood transfusion to neonates will be made solely by the clinical staff attending the infants. In Wellington NICU, there is a blood transfusion guideline to assist clinicians in deciding the timing of transfusion (see Appendix 1).

Informed parental consent will be obtained in all cases prior to data collection.

Once the parental consent is obtained, following data will be collected as part of this study:

<u>Patient characteristics:</u>
- Gestational age

- Postnatal age
- Ethnicity
- Sex
- Birth weight (customized centile)
- Weight at time of transfusion
- Haemoglobin and Haematocrit count prior to transfusion
- Respiratory support required at time of transfusion, 24hrs and 5 days after transfusion
- Caffeine treatment

Cerebral and somatic near infra-red spectroscopy (NIRS)

Cerebral and somatic regional oxygenation levels will be measured for 3hrs pre-, during and immediately post transfusion, and at 24hrs and 5 days post transfusion. Multi-site NIRS system (Nonin SenSmart™ Model X-100) with non-adhesive regional oximetry sensors will be used (EQUANOX Advanced 9004CB-NA Paediatric/Neonatal). The Paediatric/Neonatal sensors have the advantage of having a completely flat surface to avoid pressure-related injury on fragile skin of infants. They will be attached to infants using soft elastic bandages or a Tegaderm, which are routinely used in clinical practice.

The sensors will be positioned using a standard template to minimise inter-observer variability in sensor placement. The following organ systems will be studied:

Brain: Left fronto-parietal area of infant's head. Two lateral LED emitters should avoid the midline (to avoid interference by the sagittal sinus) and hair.
Liver: Point-of-care ultrasound will be performed to ensure that probe is placed adjacent to the organ
Muscle: Sensor will be placed vertically on left gastrocnemius muscle (right gastrocnemius, or quadriceps muscles may be used instead if there is a clinical reason to avoid certain locations, e.g. long-line placement, peripheral IV, recent tissue extravasation)

Cardiorespiratory stability

1. Heart rate and peripheral arterial saturation will be recorded using a pulse oximeter (MassimoRadical8™) for 12 hours prior to transfusion, during transfusion and again for 12 hours at 24hrs and 5 days post transfusion.
2. Non-invasive, continuous blood pressure monitoring will be performed using a set of soft blood pressure cuffs (Human NIBP Set™) for 12 hours prior to transfusion, during transfusion and again for 12 hours at 24hrs and 5 days post transfusion.

Position of infants

Infants will be placed supine during data collection unless medically indicated for them to lie in other positions (sleep position of infants will be recorded as part of study). This is because sleep position is known to affect parameters of cardiorespiratory stability.

Power analysis:
We calculated that a sample size of at least 24 infants is required to detect a significant increase of 10% in cerebral regional oxygenation 24hrs post transfusion with 80% power using p-value of 0.05 and the margin of error of +/- 4%.

Appendix 1: Wellington NICU transfusion guideline:

Age	Sample type	CPAP FiO2 ≥ 30%	CPAP FiO2 <30% or less support
1-7 days	Capillary Arterial/venous	130g/L 120g/L	120g/L 110g/L
8-14 days	Capillary Arterial/venous	120g/L 110g/L	100g/L 90g/L
≥15 days	Capillary Arterial/venous	100g/L 90g/L	85g/L 75g/L

For pre-discharge infants, these thresholds are reduced by 5g/L if reticulocytes are ≥30%. This is reduced further by a further 5g/L if infant is completely asymptomatic.

Irradiated and cytomegalovirus negative packed red cells are routinely used. Volume of blood transfusion is normally 15ml/kg unless a different volume is chosen for clinical reasons.