ACUTE NORMOVOLEMIC HAEMODILUTION (ANH) – INFORMATION AND SUGGESTED GUIDELINES

WHAT IS ANH?

ANH is a technique in which whole blood is removed from a patient, while circulating volume is maintained with acellular fluid. It is performed shortly before or shortly after induction of anaesthesia. ANH is a technique that may be considered in patients undergoing surgery in which substantial blood loss is anticipated.

ADVANTAGES

1. Reduces or eliminates the need for allogeneic blood transfusion.
2. Provides fresh autologous blood product compared to stored blood. It has functional platelets, normal levels of clotting factors and 2,3 DPG, and no biochemical alterations associated with storage.
3. It is the least costly method of autologous blood procurement.
4. The blood does not require testing.
5. It decreases the risk of transfusion reaction due to wrong blood administration error.
6. Eliminates the risk of infection transmission associated with volunteer donor blood (transmission risks: HIV – less than 1 in 1,000,000 per unit; Hepatitis C – less than 1 in 1,000,000 per unit; Hepatitis B – 1 in 764,000 per unit; HTLV- 1 less than 1 in 1 million).
7. Can be used in presence of malignancy or infection (peritonitis etc) where cell saver blood may be contraindicated.
8. Can be used for emergent operations where preoperative autologous donation is not possible.

INDICATIONS

1. Surgery associated with substantial blood loss (>750-1500mls).
2. Patient request for transfusion free management for religious/personal reasons. (see section below regarding Jehovah’s Witnesses)
3. Surgical procedures where a benefit from ANH has been demonstrated.
   - Radical prostatectomy
   - Hip and knee arthroplasty
   - Elderly patients without cardiac disease
   - Cardiothoracic surgery
   - Vascular surgery (AAA repair and other vascular procedures)
   - Spine surgery
   - Liver resections

For ANH to be maximally efficacious, surgical blood loss should be more than 70% of the patient’s blood volume. When the blood loss exceeds 90% of the patient’s blood volume ANH alone may not be able to prevent exposure to allogeneic blood, but it may reduce the number of allogeneic units transfused.
**CONTRAINDICATIONS**

1. Anaemia (Hb under 90 g/L). (Patients with iron deficiency anaemia can be treated with p.o. or IV iron and erythropoietin prior to surgery according to established guidelines.)
2. Impaired renal function, (unable to excrete fluid load)
3. When increased cardiac output is undesirable (e.g. coronary artery disease, aortic stenosis)
4. Clinically evident limitation of cardiac function, untreated hypertension
5. Clotting disorders.
6. Significant pulmonary disease
7. Bacteraemia

**CONSENT PROCESS**

Patients who have religious or spiritual reasons for refusing blood components should sign a release of liability form for refusal of blood transfusion. This release states the patients has been informed of the risk of refusal and also specifically what blood components, if any, the patient is willing to accept. The release must be signed by both the patient’s clinician and the patient, or their legal representative, and clearly displayed in the chart as it serves to alert others of the patient’s preferences.

**PRACTICAL APPLICATIONS PROTOCOL**

**Personnel should be immediately available who are conversant with the technique of ANH, its complications and the compensatory mechanisms it invokes.**

- Appropriate monitoring equipment must be available and used as per Departmental policy
- Blood is withdrawn after induction of anaesthesia and before the start of surgery.
  - A CVP or external jugular line is the fastest way to withdraw blood.
  - If using a Cordis to withdraw blood, make sure that the volume replacement is fast enough.
  - To avoid damage to cellular components, it is recommended to use 14-16G IVs to withdraw blood. 18 G is the minimum acceptable in adult patients.
  - The rate of blood withdrawal is not relevant as long as euvolaemia is maintained.
- Blood should be withdrawn using a strict aseptic technique
- Use of an arterial line for blood collection is not recommended as one loses the ability to monitor arterial pressure (and the wave-form for swings produced by respiration), and there is a risk of occluding the arterial catheter.
  - However, clinicians can use it at their discretion.
- Use separate IV lines to withdraw blood and infuse the replacement fluid.
  - Use fluid warmer as up to 9 liters of fluid may have to be administered over less than an hour. ANH takes about 20-35 minutes.
- Collect blood in standard transfusion bags containing anticoagulant (citrate-phosphate-dextrose-adenosine) –
  - Obtained from the theatre technicians’ room (name location).
  - Use a male-to-male connector to connect the bag to the IV.
  - A weighing scale may be used (if available)- note the weight of the bag with the CPDA and collect blood until an additional 450 gms weight.
  - Gently agitate the bag frequently to ensure proper mixing of the blood and anticoagulant
  - Once the collection is complete, clamp the collecting tubing and knot it.
- Label the bags and number them as per instructions in “labeling the blood”.
- The first 450 - 500 mls of blood can usually be withdrawn without the need for fluid replacement, after that replace blood with fluid in the ratio of 1 ml blood : 3 ml Lactated Ringers or Normal Saline or Plasma-Lyte.
- 6% Hydroxyethyl Starch (generic) and 5% albumin have also been used in a 1:1 ratio. (Note: Hydroxyethyl Starch may affect coagulation; patients who object to transfusion may not accept the use of albumin)
- High FiO₂ in the perioperative period is desirable to improve the oxygen delivery.

**LABELING THE BLOOD**

- Patient name, number, date and time
- Important to sequentially number the units as filled, if more than one is withdrawn
- Keep the blood with the patient in theatre
- THE BLOOD IS ONLY FOR REINFUSION IN THEATRE, IT MUST NOT LEAVE THEATRE (discard any blood unused at the end of surgery)
- Write “FOR AUTOLOGOUS USE ONLY” on the label

**STORING THE BLOOD**

- Store the blood in theatre with the patient. It is suggested that a little of the anticoagulant in the blood bag is introduced into the line from which the blood is withdrawn to prevent clotting.
  - **NOTE:** For use of this technique and blood storage in Jehovah’s Witness patients, see “Special Considerations in Jehovah’s Witnesses” below.
- Blood may be kept at room temperature for up to 4 hours after which time it should be stored at a preferred temperature of 6°C (see below for exceptions).
  - Note: Platelets lose function upon cooling.
- Blood bags should be agitated periodically while filling, to ensure mixing of the blood with the anticoagulant. Each bag should contain no more than 450 ml and no less than 300 ml of blood to ensure the proper ratio of blood to anticoagulant (ratio of 10:1)
- After initial agitation during collection, there is no need to rock or agitate the blood while it is being “stored” in theatre if correct collection bags have been used
- The first one to two units withdrawn are rich with inactivated clotting factors. Accordingly, based on blood loss and overall condition of the patient, the anaesthetist will determine at the end of the case whether to reinfuse those units first or last.

**VOLUME OF BLOOD TO WITHDRAW**

- **Key monitoring guideline:** *tachycardia means the patient’s threshold for phlebotomy has been reached. Stop blood withdrawal with onset of tachycardia.*
- Euvoalaemia is one of the cornerstones of proper performance of ANH. Therefore, the amount of fluid to be replaced to maintain euvoalaemia will depend upon the patient’s age, size, medical condition, hemodynamic status and the amount of blood removed.
- Hb levels should be determined following removal of blood (i.e., after haemodilution of the patient, and at regular intervals during the surgical procedure)
- The volume of blood removed will depend upon the patient’s initial Hb, estimated blood volume to be lost during the surgery, and the haemodynamic status of the patient.
  - Usually between 2 – 4 units (approx 400-500 mls /bag)
  - Maximum recommended volume 2000mls
Theatre target =
1. Until patient reaches phlebotomy threshold or equivalent to expected blood loss and quantity that would be normally needed in allogeneic infusions or haematocrit of 20%
   
   Calculation for volume of blood to withdraw\(^9\)
   \[
   \text{Vol} = \frac{\text{EBV} \times (\text{Hi} - \text{Hf})}{\text{Havg}}
   \]

   Hi = initial haematocrit. Hf = target haematocrit.
   Havg = average haematocrit = \((\text{Hi} + \text{Hf})/2\)
   EBV = estimated blood volume as per table (can use body weight x 65 ml for women and 70 ml for men)

   • Once the period of major blood loss is over, or earlier if clinically indicated, the blood is slowly transfused back to the patient in the conventional manner.
   o The units are usually transfused in the reverse order of collection. The first unit removed, which has the highest Hb level and the most platelets, is transfused last.
   o This is based on the assumption that all units removed will be returned.

PAEDIATRIC PATIENTS
1) All of the above policies and procedures for ANH should be strictly followed for this patient population.

2) A patient’s total estimated blood volume (EBV) will be calculated based on patient’s weight and age.
   o The following formulas will be used to estimate the blood volumes and blood losses
     - EBV = 95 ml/kg for premature neonates
     - EBV = 90 ml/kg for full term neonates
     - EBV = 80 ml/kg for infants to one year
     - EBV = 60 - 70 ml/kg for one year plus

3) The amount of blood withdrawn for ANH will be dependent on the patient’s total blood volume and weight.

4) When using adult blood bags for pediatric cases, it is necessary to withdraw an amount of citrate from the bag proportional to the amount of blood being collected. This is to keep the whole blood to citrate ratio approximately equal to 10:1.

OBSTETRICAL PATIENTS
1) All of the above policies and procedures for ANH should be strictly followed for this patient population.
2) ANH should be considered an alternative to allogeneic blood transfusion and should be used in cases where substantial blood loss is anticipated (i.e., placenta previa, placenta accreta, etc...) and in cases where patients have developed antibodies to blood.

3) Patients undergoing both regional anaesthesia and ANH should be given special consideration regarding their intravascular volume and fluid status.

**ANH, FLUID REPLACEMENT AND COAGULATION ABNORMALITIES**

1) For cases where moderate to severe haemodilution is planned (750 ml – 1500 ml or more), the anaesthesia team should anticipate the rare possibility that a coagulopathy may develop during the case.

2) The type of replacement fluid should take the above into consideration. *In vivo* and *in vitro* studies have shown that moderate to severe haemodilution with hydroxyethyl starches as the replacement fluid may cause an alteration in platelet function, or a negative effect on blood coagulation factors in addition to the effects of haemodilution on the haemostatic function.(24) This does not necessarily translate into abnormal clinical bleeding.(25) Surgery itself, without ANH, can induce a significant increase in markers for activation of the coagulation system and fibrinolysis.(3) In addition, severe haemodilution secondary to blood loss replaced with crystalloids or colloids (without ANH) can also lead to a coagulopathy.

3) Measures to prevent coagulation abnormalities

   o Fractionation of the blood removed and then returning approximately ½ of the fractionated fluid, both platelet rich plasma (PRP) and platelet poor plasma (PPP), while the ANH process is still ongoing.

   o This is to prevent a dilutional coagulopathy that may rarely develop as a result of moderate to severe ANH, and the process of ongoing dilution from blood loss and replacement of this blood loss with intravenous fluid.

   o Fractionation and returning a portion of the platelet poor plasma and platelet rich plasma limits the need for excessive use of intravenous fluids, thus preventing a dilutional coagulopathy.

   o Limit the amount of hydroxyethyl starches used as the replacement fluid (1000cc – 2500cc) during ANH.

      ▪ Studies have shown that using amounts greater than 20 ml/kg does not increase the risk of bleeding in cases with major blood loss.(25)

      ▪ Studies have also shown that the use of hydroxethyl starches as replacement fluids during moderate to severe ANH may cause platelet adhesion abnormalities and a decrease in factor VIII:C.(24)

      ▪ Given the above, there is no current algorithm to predict which patients are likely to develop a coagulopathy from ANH. Severe blood loss with ongoing dilution may be the best predictor.

4) Below are goal directed steps to minimise the negative effects of severe haemodilution with or without the use of hydroxyethyl starches.

   o Use the thromboelastography a goal directed guide to the coagulation status if the anesthesia team removes > 1500 ml of blood during ANH.
- Baseline thromboelastography.
- Post ANH thromboelastography (+/- the return of ½ the PRP and PPP).
- Follow thromboelastography every few hours or if there is a concern that the patient appears clinically “oozy”.
- Give goal directed therapy depending on the thromboelastography results.
- Remember that the PRP and PPP can be used to correct thromboelastography abnormalities.
  - Switch to crystalloids or minimise the use of hydroxyethyl starches (1-2 liters) in the face of ongoing blood loss and concern about platelet abnormalities.
  - Prophylactic DDAVP in cases where hydroxyethyl starch was used.
  - Return remaining PPR and PPP

**SPECIAL CONSIDERATIONS FOR JEHOVAH’S WITNESSES**

In general, Jehovah’s Witness patients request that their blood not be withdrawn and “stored”. Witness patients who accept ANH have individual requirements about how the procedure is performed. Some request that the blood withdrawn be kept in continuity with the their circulatory system. In such cases, after the blood is withdrawn into a CPD bag, a multi-infusion port is suggested for withdrawing more than one bag of blood so that all units can be kept attached to the patient. **Confirm that this is acceptable to the patient beforehand.**

**REFERENCES**