

## PLASMA EXCHANGE: INTRODUCTION AND GUIDELINES

Original 2003 Revised April 2006 by Jed Smithyman

### INTRODUCTION

Plasma exchange is used to remove circulating toxins or to replace missing plasma factors. Treatment usually requires a 60 mL/kg exchange volume (with a practical maximum of 4 L over 3-4 hours) daily or intermittently, for up to 10 days.

UCH ICU, plasma exchange is performed using a technique similar to haemofiltration and using the same equipment (plasmafiltration), except that the plasmafilter membrane is highly permeable (molecular weight cut-off typically < 1 million daltons).

### INDICATIONS:

Examples of diseases treated with plasma exchange:

5 main groups

- 1) Antibody-mediated diseases:
  - Antiglomerular basement membrane antibody disease (Goodpasture's syndrome)
  - Myasthenia gravis
- 2) Immune complex-mediated diseases:
  - Wegener's Granulomatosis
  - Cryoglobulinaemia
  - Systemic lupus erythematosus
- 3) Presumed immunological diseases:
  - Guillain-Barré syndrome
- 4) Thrombotic Microangiopathies (Thrombotic thrombocytopenia purpura / Haemolytic Uraemic Syndrome [TTP/HUS])
  - Post-partum
  - Drug-induced (cyclosporin, mitomycin)
  - Bone marrow transplantation
- 5) Miscellaneous:
  - Poisoning (paraquat, mushrooms)
  - Sepsis (meningococcaemia)
  - Acute pancreatitis due to chylomicronaemia

In the treatment of acute or chronic autoimmune disease, the aim is to minimise irreparable end-organ damage, and to support the patient during the acute phase.

The exchange volume is usually 3 litres, at a rate of 1 to 1.5 litres per hour. During plasma exchange there is progressive dilution, and decreasing efficiency as some components remain in the intravascular space. Therefore daily exchanges are preferable to longer or infrequent exchanges, and should be gauged according to the response to therapy.

### PRINCIPLES UNDERLYING PLASMA EXCHANGE THERAPY

#### DELIVERY OF CARE

The nurse in charge will ensure that the care is delivered or supervised by a nurse with CRRT experience and (ideally), with plasma exchange experience.

#### TRAINING

Education and training is via the ICU teaching programme, the Introduction to ITU course, the BSc critical care module, working with mentors and clinical teachers, and Unit study days. Teaching is co-ordinated by the clinical education and practice development staff, assisted by the CRRT working group.

#### RESOURCES

- Guidelines for correct installation of sets and troubleshooting to be available in hardcopy and/or Intranet.
- ICU Standards of Care – Patients undergoing Plasma Exchange.
- Senior staff.

## CHOICE OF REPLACEMENT FLUID

The choice of replacement fluid may be dictated by the pathology involved, and will be prescribed with advice of haematologists, physicians and intensivists.

The choices are :

- **Crystalloid** – can only be given as 20-40% of volume, with remainder being a colloid.
- **Human Albumin Solution**– expensive.
- **Synthetic colloid**, e.g. gelofusine, eloHAES
- **Fresh Frozen Plasma** – limited resource. A replacement regimen consisting entirely of FFP may be indicated where the exchange is performed to replace missing plasma factors, as in HUS/TTP. Some FFP may be added into the replacement regimen at the end of the exchange when the removal of clotting factors poses a particular risk, e.g. after an invasive procedure or in the presence of alveolar haemorrhage.
- **Cryosupernatant** – may be appropriate in certain types of TTP, and should be discussed with the duty haematology SpR

Typical regime at UCLH for 3 litre exchange:

- 1) 2.5 litres of colloid (Gelofusine alternating with eloHAES)
- 2) 2 units of FFP at the end

## ANTICOAGULATION

As for haemofiltration. The patient's clotting should be reviewed prior to therapy. If the clotting is normal, heparin may be administered. The patient's clotting may be grossly abnormal and, as the therapy only lasts 3 hours, it may be possible to complete without anticoagulation. Plasma exchange depletes platelets and fibrinogen as well as clotting factors. Plasma exchange sessions should be withheld if thrombocytopenia develops during the course of treatment (platelet count  $< 70 \times 10^9/L$ ), **except when treating TTP-HUS**. FFP is given last to avoid filtering the clotting factors in the fresh plasma.

Patients receiving plasma exchange performed by Haematology staff using the cell separating centrifuge will receive some of the sodium citrate anticoagulant, which may lead to hypocalcaemia, requiring calcium supplementation.

## FLUID BALANCE

Usually a volume is given back equal to that removed unless the patient is already severely overloaded. It is important to keep up the replacement fluid with the amount taken off to avoid hypotension. Return the patient's blood if possible at the termination of treatment.

## HAEMODYNAMIC MONITORING

- Check clotting/FBC before and after therapy.
- Continuous ECG, blood pressure, and CVP monitoring is essential to detect hypotension or dysrhythmias.
- Blood gas analysis to monitor serum potassium as it will be removed with plasma.

Monitor temperature and maintain at  $>36^\circ\text{C}$ . Loss of body heat through extra-corporeal circulation may require warming with warming blanket.

## ACCESS

Same as CRRT.

- Always check that each port is able to be aspirated and flushed easily before the commencement of therapy, and if there are problems with getting the filter to run. If it is not easy to draw back and flush, then the vascath must be repositioned.
- Always draw back before flushing to avoid injecting a clot into the patient.
- Aseptic technique is required when attaching/detaching lines to ports.
- Dressing of vascath site is per Unit policy.
- UCH ICU each lumen of the vascath is locked with 5 ml of 0.9% saline between treatments.
- 5 mL of blood must always be drawn back and the syringe discarded before flushing the vascath with saline, to remove heparin or clots. Do not spray blood onto gauze to check for clots, this is a dangerous practice as it risks a splash injury.

## PUMP SPEED

Pump speed is slower than CRRT as the fibres in the filter are more delicate. The circuit is flushed at 100 mL/min, and treatment carried out at a maximum of 150 mL/min.

- If possible, the vascath should be visible in case of disconnection or displacement, to avoid the risk of haemorrhage or air embolism.
- The arterial and venous lines should be supported by clamps to prevent dragging on the vascath.
- Aseptic technique must be used when redressing the vascath site, connecting and disconnecting the set, priming the circuit or changing the replacement or dialysate fluid bags, to avoid the risk of infection. Plasma exchange depletes immunoglobulins, making the patient more susceptible to infection.
- Observe access sites, NG aspirate for sign of bleeding due to over-anticoagulation.
- The wearing of face-masks/goggles and gloves is absolutely essential when connecting/disconnecting the circuit or changing the ultrafiltrate/effluent receptacle.
- Dispose of used filter circuits and effluent bags in yellow bins.

## DRUG DOSAGES

Plasma bound drugs will be removed with the plasma. Delay giving medications if possible until completion of therapy.

# GUIDELINES FOR THERAPEUTIC PLASMA EXCHANGE

Initial set up is the same as for CRRT.

Turn on machine. Choose patient: confirm. Choose TPE.

Follow instructions on screen.

Insert filter cartridge, place replacement line, the 4 pressure pods, and the effluent line. Hang the effluent bag on the scales. Route access line through guides, attach to prime collection bag and hang on Left hook. Insert return line through air detector and return line clamp, then load set.

Hang priming fluid (saline) on Right hook.

Install anticoagulant syringe into syringe driver.

Hang replacement fluid on replacement scale (for priming use 1 litre bag of saline).

Return line is attached to priming fluid bag.

Effluent line is connected to effluent bag.

Check access line connection to prime collection bag is tight.

Unclamp clamped lines, press PRIME.

Automatic priming sequence primes for first litre of saline. You will have more problems with air during priming for TPE than with CRRT, but it will be cleared as you prime with 4 litres altogether.

At the end of first priming cycle, you will get the message: “1 of 4 priming cycles complete.” Remember to press “Reprime” after you hang the second litre of saline. If you press “Continue” the machine will go into “Self Test” mode.

The set should be primed with 4 litres of saline, and the last litre should be heparinised with 5000 i.u. heparin if this is not contraindicated.

If there is a problem, or if the filter is left for a while, it is recommended to reprime with another bag of saline rather than use a manual prim from fluid remaining in the last bag as you risk getting air in the circuit. (If the filter is left sitting for a while the ethylene glycol preservative may migrate back out of the fluid, to the detriment of the patient).

On the last litre do lots of tapping and tweaking to get the air out.

**TRANSMEMBRANE PRESSURE:** is monitored at the top of the the filter, whereas in CRRT it is measured as an average over the filter. Higher pressures pull the red blood cells hard against the pores causing rupture and haemolysis, and the circuit may fail before the treatment is completed due to the constant TMP alarms.

At completion of the fourth litre prime, press CONTINUE and PRIME TEST is initiated, which takes longer than in CRRT as it includes the calibration of TMP pressure. At the end of priming you may hear the dialysate pump making a funny noise, which is the machine checking that it is a plasma filter that is installed.

Then go to PAGE 1: TP prescription.

PAGE 2: Flow rates

## PRESCRIPTION PAGE:

- Enter patient's pre-treatment haematocrit (the most recent) converted to per cent. (for example if the Lab HCT is 0.33, this is 33%. The machine has a default HCT value of 43%).
- Enter PLASMA VOLUME to the total required volume of exchange (usually 3 litres but this may vary with size of patient and disease process).
- Enter the volume of the first container of fluid you are going to use (crystalloid/FFP/albumen/synthetic plasma substitutes. You need to enter a slightly lower volume than actually in the container to avoid getting air in the circuit. With albumen you need to underestimate the volume in the bottle by 30 ml e.g. enter 370 ml for 400 ml because of its specific gravity, its tendency to froth up and the increased risk of getting air in the circuit. FFP is more accurately measured, so you only need to enter 10 ml less than the total volume on the bag to avoid getting air in the circuit.)

## FLOW RATES:

- **Anticoagulant:** set rate. TPE requires more anticoagulation than CRRT e.g. 5000 – 10000 i.u. as a bolus loading dose followed by 15 iu/kg/hour rather than 10 i.u./kg/hour as an infusion.
- **Plasma Removal Rate:** is set to zero
- **Blood Flow:** start at 100 ml/min, this is the minimum blood flow rate for TPE.
- **Plasma Replacement:** the volume exchanged each hour) – start at 250 ml/hour.

START SLOWLY TO AVOID COMPROMISING THE FILTER MEMBRANE EARLY ON.

PLASMA REMOVAL RATE should always be zero unless there are exceptional circumstances. If you take off fluid, you are taking off plasma, not plasma water, and the patient should not be plasma negative. To take off water the patient needs CRRT not TPE.

If you want to change the prescription after you've started, you can go back and change it, if something has changed or you want to alter the total volume of the exchange.

Press CONTINUE when you're ready. Clamp both lumens of the access (red) line at the collection bag, and clamp the return (blue) line. Before connecting to the patient there are 3 things you need to do:

- 1) Empty the effluent bag before you start so that if you need to take a plasma sample from the bag it won't be contaminated by saline, and so that you don't have to do it during the exchange.
- 2) Change the litre bag of saline that you hung on the replacement side for priming to whatever fluid you are using for the exchange. The spike should have a blue cap on the side to open as an air inlet if you are using bottles.
- 3) Connect a giving set and a bag of saline to the extra limb on the access line, which you can drip in (you don't need a pump) to nurse the circuit along if the transmembrane pressure starts rising. If your patient is anuric you might want to be cautious with how much fluid you give like this; if they're passing urine, it doesn't matter. If your patient becomes calcium compromised during the treatment, you can attach a syringe of calcium gluconate to this lumen to give boluses as required.

CONNECT PATIENT: take red line off prime collection bag, connect to arterial port of vascath, take blue line off priming solution bag, and attach to venous port of vascath. Observe patient. Unclamp lines.

Press START.

The blood pump starts.

The replacement pump starts.

If the catheter pressures (e.g. ACCESS/RETURN) allow, increase blood pump speed, aim for 150 ml/min, you can go higher if you want. Observe the patient for anaphylaxis, hypotension.

The key thing is to keep observing the transmembrane pressure which usually starts around the 40 mmHg mark. If the patient is tolerating the process and the TMPa stays around 40 mmHg, you can go back to your SET FLOW RATES page and increase the exchange rate (you'll notice the TREATMENT TIME will change with the alteration in the flow rates, the higher the flow rate, the shorter the treatment.). Go to REPLACEMENT and increase the flow to 500 ml/hour, looking at the TMPa to make sure it stays around 40 mmHg. Go up by 250 ml/hour at a time, monitoring the TMPa as you do. If you see the TMPa rising to 50-60 mmHg, step the replacement rate down by 250 ml/hour, and try again in a minute or so, dripping in some saline (slowly) through the giving set on the extra lumen. Once you have started exchanging, drawing off some of the patient's plasma and giving the clean plasma substitute, the exchange should get easier as less debris is being deposited on the membrane. If you're careful, if you don't push the filter too much, although the TMPa rises initially, sometimes it will drop again as clean plasma circulates.

Aim to take the REPLACEMENT rate up to 1500 ml/hour maximum. Treatment can not continue if the TMPa reaches 100 mmHg.

Keep observing the patient for anaphylaxis, hypotension, hypocalcaemia, hypothermia. (NB: hypocalcaemia causes depressed cardiac function, prolonged QT interval, loss of vasomotor tone, muscle weakness, paraesthesia, and tetany.

Treatment is 10 ml of calcium gluconate 10% slow IV bolus over 3 minutes).

REPLACEMENT CONTAINER EMPTY: press CONTAINER VOLUME, then you have to adjust the volume of the new container and CONFIRM, or CONFIRM that the volume is the same as the previous container, then press CONTINUE (i.e. It has to be CONFIRM, then CONTINUE). Always enter at least 10 ml less volume than that actually in the container to avoid getting air in the circuit. If it looks like you miscalculated and the fluid is running out and air is about to enter the circuit, quickly press MORE SOFT KEYS and CHANGE BAGS.

ACTUAL PLASMA LOSS should be zero, but you sometimes end up with a number at the end of treatment, because of alarms interfering with the treatment. Using albumen can cause it to appear that there is a negative plasma balance, whereas FFP is more accurate: this is related to the relative specific gravity of the fluids.

ACCESS and RETURN PRESSURE ALARMS are the same as for CRRT and require the same response.

If there is a TMP TOO HIGH alarm the blood pump will carry on running, as this is only a caution alarm, but you won't be able to start the treatment. Decrease the REPLACEMENT rate and/or PATIENT EXCHANGE VOLUME (decrease to 1000), and press CONTINUE. This doesn't always solve the problem; once the TMP alarm starts it usually remains problematic through the treatment.

END OF TREATMENT: at the end, change start time back to when you started the treatment (with the down arrow), and set end time forward as far as the treatment went, and you'll get the total volume of the exchange.

When you get to the end of the treatment and you have delivered the volume of the plasma exchange that you have requested at the start, you will get a message: CAUTION: TP PRESCRIPTION DELIVERED. You can either stop there and take the set down, or if you still have some FFP you want to give press CONTINUE and the machine will carry on giving the fluid; it will still tell you when your containers are empty but it won't give you any more alarms to say the treatment is complete.

If TMPa is too high or excessive you will have to stop and disconnect. If you are going to change the set and carry on, set up in Same Patient, and the treatment data is retained.

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