GUIDELINE FOR THERAPEUTIC PLASMA EXCHANGE VIA PRISMAFLEX

1.0 PURPOSE

To provide guidelines on therapeutic plasma exchange (TPE) for children in CICU.

2.0 POLICY

This policy defines the indications of TPE, the procedures involving the operation of the Prismaflex machine as well as the care and monitoring of patients on TPE

The decision to initiate TPE is made by the patient's primary physician, based on the indication outlined in 4.0.

2.1 Doctor in charge (Associate Consultant and above) in CICU prescribes the TPE order.

2.2 Staff Nurse in CICU will prepare, prime, initiate and terminate the therapy via the PRISMAFLEX machine using the filtration method.

2.3 CICU trained Nurse will perform nursing management and monitor patient on TPE

2.4 Each patient is assessed, on an individual basis, to the need for starting TPE, the number and frequency of sessions, by the intensive care physician with the primary doctor

3.0 DEFINITION

TPE is an extracorporeal blood purification technique designed for the removal of large molecular weight substances from the plasma. TPE involves the separation of plasma from the whole blood and the infusion of a replacement fluid in equal volume to the plasma that is removed. The replacement fluid can be in the form of 5% albumin, a mixture of albumin and 0.9% saline or fresh frozen plasma (FFP). With TPE, red blood cells, white blood cells and platelets are returned to the patient

3.1 The mechanisms by which TPE exerts its therapeutic effects are summarized as:

3.1.1 Removal of abnormal circulating factor

- Antibody (anti-GBM disease, Myasthenia gravis, Guillain-Barré syndrome)
- Monoclonal protein (Waldenstrom's macroglobulinemia, myeloma protein)
- Circulating immune complexes (cryoglobulinemia, SLE)

3.1.2 Replenishment of specific plasma factor

- thrombotic thrombocytopenic purpura

3.1.3 Other effects on immune system

- Improvement in function of reticuloendothelial system
- Removal of inflammatory mediators (cytokines, complement
- Shift in antibody-to-antigen to more soluble forms of immune complexes
- Stimulation of lymphocyte clones to enhance cytotoxic therapy

3.2 TPE have been shown in the following diseases to be of clinical benefit either as a primary an adjunctive therapy

- Goodpasture's syndrome (anti-GBM disease)
- Thrombotic thrombocytopenic purpura syndrome
- Hemolytic uremic syndrome

- Cryoglobulinemia
- Hyperviscosity syndrome
- Myeloma cast nephropathy
- Acute demyelinating polyneuropathy (Guillain-Barré)
- Chronic inflammatory demyelinating polyneuropathy
- Homozygous familial hypercholesterolemia (selective adsorption)
- Myasthenia gravis crisis
- Chronic inflammatory demyelinating polyneuropathy
- Eaton-Lambert myasthenic syndrome
- Post-transfusion purpura
- Refsum's disease
- Cutaneous lymphoma (photopheresis
- HIV-related syndromes (polyneuropathy, hyperviscosity, thrombotic
- Coagulation factor inhibitors
- Paraproteinemic peripheral neuropathy
- Systemic vasculitis associated with ANCA
- Rapidly progressive glomerulonephritis (without anti-GBM)
- SLE (in particular SLE cerebritis
- ABO-incompatible marrow transplant
- Bullous pemphigoid
- Pemphigus vulgaris
- Immune thrombocytopenia (Staph protein A adsorption)
- Hemolytic disease of the newborn

3.3 *EQUIPMENT*

PRISMAFLEX machine

The dialysis machines which are able to perform the TPE using the 'TPE' function
The method uses plasma separation by a highly permeable membrane, TPE 1000 or TPE2000.

Plasma Membrane

.	TPE1000	TPE2000
Membrane	polypropylene	polypropylene
Surface area	0.15m^2	0.35m^2
Wall thickness	150 µm	150 µm

Extracorporeal volume

	Blood line (ml)	Plasma filter (ml)
TPE1000	71	23
TPE2000	125	41

Filter size

	TPE 1000	TPE 2000
Patient's weight	<30kg	>30kg

Blood flow rate (Qb)

TPE1000: minimum blood flow rate 50ml/min, maximum blood flow rate

TPE2000: minimum blood flow rate 100ml/min, maximum blood flow rate

QB (ml/min)	Maximum Plasma filtration rate (ml/min)	
	TPE1000	TPE2000
50	16	-
100	29	42
180	49	-
200	-	79
250	-	97

3.4 *SITE OF VASCULAR ACCESS*

Vascular access is achieved by the insertion of a dual-lumen catheter into the femoral, internal jugular or subclavian veins. Femoral catheter is preferred especially with the use of citrate anticoagulation, as the return of hypocalcaemic blood near the AV node may cause arrhythmia when using the neck veins

3.5 *SIZE OF VASCULAR ACCESS*

As the minimum blood flow of 50ml/min is required, a catheter size of <7F may not support this flow. The table below serves as a guide to the size of catheter based on body weight.

Weight of patient (Kg)	**Cannula size**
Neonate	Single lumen 5F
	Double lumen 6.5F
3-6	Double lumen 6.5F
6-15	Double lumen 8F
15-30	Double lumen 10F
>30	Double lumen 11F
	Triple lumen 13F

3.6 *VOLUME EXCHANGE*

3.6.1 **Estimated plasma volume (EPV)**

The estimated plasma volume (EPV) can be calculated by the following formulae:

EPV (ml) = (1 – HCT) (b + cW)

W = lean body weight,
b = 1530 for males, 864 for females and
c = 41 for males, 47.2 for females
HCT = haematocrit

3.6.2 **OR**

EPV (ml) = [TBV (ml/kg) × body weight (kg)] × (1 – HCT)

Where TBV is the total blood volume
TBV = 80ml/kg in children <10kg
TBV = 70ml/kg in children ≥10kg

3.6.3 Relationship of plasma exchange volume with removal

PV Equivalents	Substance removed (%)	Post-exchange level (%)
0.5	35	65
1.0	55	45
1.5	65	35
2.0	70	30

The kinetics of immunoglobulin removal by TPE follows an exponential relationship

$$C_t = Coe^{-x}$$

where Co is the initial concentration of the substance, Ct is its concentration at time t, and x depends on the volume of distribution of the substance in question
The first plasma volume removed results in 55% of the substance removed and the second plasma volume removed results in an additional 15% of the substance being removed. At most two, plasma volumes are removed at each TPE session
Rate of plasma removal should be <50 ml/kg/hr

3.7 *REPLACEMENT FLUIDS*

Colloidal agents are used as replacement solutions in the form of 5% albumin, 5% albumin with normal saline or FFP.

Albumin	5% Albumin
FFP	Indications for FFP as partial or total replacement fluid: • TTP/HUS • preexisting coagulopathy, • risk of cholinesterase depletion • when the fibrinogen level is low (< 1.25g/L)

If albumin is used as the replacement fluid:
Plasmapheresis depletes coagulation factors, replacement by albumin and crystalloids alone may deplete these factors. If there are multiple sessions over short periods, FFP should be used for the last 1/3 of replacement fluid.

3.8 *COMPLICATIONS*

Complications can be classified as:

3.8.1 *Related to vascular access*
- Hematoma
- Pneumothorax
- Retroperitoneal bleed

3.8.2 *Related to the procedure*
- Hypotension from externalization of blood in the extracorporeal circuit
- Hypotension due to decreased intravascular oncotic pressure
- Bleeding from reduction in plasma levels of coagulation factors
- Oedema formation due to decreased intravascular oncotic pressure
- Loss of cellular elements (platelets)
- Ethylene oxide-associated hypersensitivity reactions

3.83 *Related to anticoagulation*
- Bleeding, especially with heparin
- Hypocalcaemic symptoms (with citrate)
- Metabolic alkalosis (with citrate)

3.9 *STRATEGIES TO PREVENT SOME OF THESE COMPLICATIONS*

3.9.1 Hypocalcaemia
10% calcium chloride (0.2ml/kg, max 10ml) or 10% calcium gluconate (0.5ml/kg, max 20ml) is given as an infusion for the duration of the therapy, with iCa monitoring.

3.9.2 Hypokalaemia
Serum potassium should be monitored and replaced accordingly.

3.9.3 Sensitivity to replacement fluids

If there is transfusion reactions to FFP that is used as replacement fluid, evaluation should be done as per the hospital's transfusion reaction protocol
If repeated TPE sessions are required for sensitized individuals, premedications may be considered:

- PO prednisone or IV hydrocortisone (for patients who are nil by mouth),
- PO or IV diphenhydramine
- PO or IV ephedrine

3.9.4 Infections post TPE

IVIG (0.5g/kg) infusion can be considered for infections, especially if the serum IgG level is low

3.9.5 ACE Inhibitor

Consider stopping ACE inhibitors 24-48 hours prior to TPE

3.9.6 Haemorrhage

Use FFP as replacement fluid at the last 1/3 of session

3.10 *MONITORING*

3.10.1 Vital signs

- Continuous heart rate and ECG monitor
- Hourly BP

3.10.2 Blood investigations

Baseline (before TPE)	PT/PTT, ACT, FBC, Blood gas, ME/iCa
During TPE (hourly)	ACT, ME/iCa
Post TPE	PT/PTT, ACT, FBC, ME/iCa

3.10.3 Monitor for haemolysis

Monitor access transmembrane pressure (TMPa). TMP should not be higher than the maximum shown in the table for the blood flow rate

Qb (ml/min)	Maximum TMPa (mmHg)	
	TPE1000	TPE2000
50	100	-
100	140	120
180	190	-
200	-	171
250	-	193

Check effluent for red or pink tinge

4.0 PROCEDURE

4.1 Informed consent (TPE info sheet)
Informed consent must be obtained before the implementation of TPE

4.2 Vascular access
Vascular access is obtained by the intensive care registrar, associate consultant or consultant by aseptic technique

4.3 TPE Order Sheet
The intensive care physician inputs the TPE orders into the TPE order sheet (Annex 1)

4.4 Medications
All medications should be reviewed by pharmacist. Medications that are highly protein-bound should preferably be given after plasmapheresis

4.5 Priming of TPE circuits using PRISMA machine
Requisites
- TPE set (select according to patient's weight)
- Normal Saline 0.9% 1000ml soft bag x 3 or 2 (for TPE 1000)
- Injection Heparin Sodium 1000unit / ml X 10 vials
- Syringe 10mls x 1
- Syringe 50ml x 1Needle 23G x 1
- Sterile gloves
- Sterile towel
- Alcohol swabs x 5

4.6 Steps in Procedure
- Perform medical hand washing
- Counter-check doctor's order in TPE order sheet
- Prime set when ready to start treatment
- Perform medical hand washing
- Open TPE set

4.7 On the PrismaFlex machine
- Select new or same patient
- When choosing therapy, select TPE mode
- Load the TPE set onto the machine and follow the step-by-step instructions on the screen.
- **TPE 1000**- 1st prime with Normal Saline 0.9% 1000ml then add 10,000 units to 2nd Normal Saline 0.9% 1000ml priming bag
- **TPE 2000**- 1st and 2nd prime with Normal Saline 0.9% 1000ml then add 10,000 units to 3rd Normal Saline 0.9% 1000ml priming bag
- Inspect the set for air and observe closely for leakage at joints and connections within the system during priming.
- Once the priming process is completed and the "self-test" is passed, the machine is ready for use.
- Press "CONTINUE" key ONLY when patient is ready to start TPE

4.8 Initiation of TPE via central venous catheter (Vascath)
- Doctor to be present before initiating treatment
- Before the procedure, the nurse should
  - Counter-check and key-in TPE order on the PrismaFlex machine with another RN.
    - Assess and record patient's haemodynamic status
    - Assess catheter site for redness and swelling
- Put on mask and apron

- Perform medical hand washing
- Prepare the following in a sterile dressing set:
  - Don on sterile gloves
  - Pour normal saline 0.9% into the compartment
  - Pour in cleansing solution
  - Add in the syringes and gauze
- Drape catheter site with sterile towel.
- Scrub the arterial and venous lumen of the catheter access ports one at a. time with chlorhexidine 2% with alcohol 70% for one minute
- Remove catheter caps and discard
- Connect a 3ml syringe filled with 1ml 0.9%NaCl to arterial port (red).
- Aspirate 1.5 ml of blood and spread the blood onto a piece of gauze to check for blood clots.
- Flush with 3ml of 0.9%NaCl into the catheter and clamp with positive pressure.
- Repeat steps for the venous port (blue).
- Connect arterial and venous lines and ensure that there is no air bubble within the line.
- Release all clamps on access lines.
- Initiate TPE treatment as per Doctor's order.
- Secure lines with micro-pore tape.

4.9 Set Prismaflex settings

- Patient's haematocrit
- Start blood flow 50mls/min and increase slowly to target (Inform Dr if not possible)
- Enter Total Replacement volume= Total Plasma volume to be exchanged
- Replacement flow ml/hr will be total replacement volume divided by the number of hours to complete.
- Plasma loss rate and pre blood rate should be kept at 0 ml/hr
- Anticoagulant rate to refer to TPE order sheet (Annex 2) anticoagulant guideline
- During change of Albumin bottle/FFP
  - Key bag change
  - At the Change Bags/Containers screen, key the volume at **Allowed Volume Replacement- ml**
    - If 500ml of 5%Albumin use, to set rate at 480ml
    - If FFP use, to set 10-20ml less than volume shown on the FFP bag

4.10 Termination of TPE from PRISMA machine

- Put on mask and apron.
- Prepare the followings in a sterile dressing set:
  - Open and put in all stopcocks, syringes, needles, and transparent dressing
  - Perform handwashing before putting on sterile glove
  - Prepare heparinised saline to heparin lock lumens of dialysis catheter
    < 5kg –330 units in 10mls normal saline (33u/ml)
    > 5kg – 1000units in 10mls normal saline (100u/ml)
  - Prepare 2 x 3ml syringes with the prepared heparinised saline
  - Filled the 2 x 5m syringes with 0.9% NaCl
  - Termination is operated through the interactive display screen
  - Standby mode is automatically entered when pressing the stop button on. the Status screen
  - Select "END TREATMENT" from the screen
  - To return blood to the patient, select "RETURN BLOOD" from the next screen
  - Follow the instruction on the "RETURN BLOOD" screen
  - Select "DISCONNECT" if end treatment without returning blood. Follow instruction
    - on the "DISCONNECT PATIENT" screen
    - Hang the bag of 0.9% NaCl at lower left corner of PrismaFlex machine
    - Clamp the access port (red) of patient's catheter
    - Clean connecting section with chlorhexidine 2% with alcohol 70% for one minute
    - Disconnect access line from patient

- Attach 5ml syringe to access port
- Unclamp the access port
- Aspirate 2 – 3 mls of blood from the lumen
- Squelch aspirate on gauge to check for any blood clot
- Flush access port with 0.9% NaCl and clamp with positive pressure
- Check patient's catheter to determine the amount of heparin to be
- injected. The volume should not exceed the amount indicated on the lumen
- Heparin lock lumen and clamp port
- Cap lumen with stopcock
- Connect access line (from PrismaFlex machine) to the bag of saline using spike
- Hold down "START RETURN" key on the screen to return desired amount
- WARNING: Do not return blood if clotting is present in blood
- of blood lines or filter
- Repeat steps with the venous port (blue)
- Change dressing at exit site if soiled or wet
- Secure the catheter down with micropore tape to keep it from dangling and to prevent dislodgement
- Press "CONTINUE" key on screen
- Press "UNLOAD" to unload pump segments from pump raceways from the next screen
- Clamp all lines attach to bags
- Disconnect lines from all bags.
- Remove and discard the set, solution bags and effluent bag
- Press "TREATMENT HISTORY" to view treatment history data from the last 24 hours.
- Record post TPE parameter
- Turn off machine and power point
- Wipe the machine with medic wipe before storage

Annex 1

PRISMA TPE ORDER SHEET

Weight (kg)		**Height (cm)**	_____	**BSA (m^2)**	_____
Allergy		**Date**	_____		
Catheter		_____Fr	_____cm	**Site**	_____
Filter	TPE 1000	TPE 2000			
Mode	TPE				

Blood flow (ml/min) 4-5ml/kg/min TPE1000:50ml/min, max180ml/min TPE2000:100ml/min; max 250ml/min	Start at	_____	Target	_____

Estimated Plasma Volume (EPV) = _____ml

The estimated plasma volume can be calculated by the following formulae:

EPV (ml) = (1 – HCT) (b + cW)
W = lean body weight,
b = 1530 for males, 864 for females and
c = 41 for males, 47.2 for females
HCT = haematocrit

OR

EPV (ml) = [TBV (ml/kg) × body weight (kg)] × (1 – HCT)
Where TBV is the total blood volume
TBV = 80ml/kg in children < 10kg
TBV = 70ml/kg in children > 10kg

Plasma volume to be exchanged = _____X **EPV**
= _____ml

NB: Do not do more than 2 plasma volume exchanges

Replacement Fluids

FFP (ml)	**5% albumin (ml)**	**Albumin with saline (ml)**

Indications for FFP as partial or total replacement fluid:

- TTP/HUS
- preexisting coagulopathy,
- risk of cholinesterase depletion
- when the fibrinogen level is low (< 1.25g/L)

Priming solution (**Avoid blood prime)**	TPE 1000	1st prime: 1000 ml x 1 normal saline	2nd prime: 1000 ml normal saline (Add 10,000U heparin)
	TPE 20000	1st and 2nd prime: 1000 ml normal saline	3rd prime: 1000 ml normal saline (Add 10,000U heparin)
Anticoagulation	Dilute _____U heparin in 50ml N/S (Amt= Wt(kg)x2.5Ux50) 1ml/hr=2.5U/kg/hr		
Loading	Bolus 20U/kg; 8ml of 50ml syringe		
Maintenance **ACT Monitoring (baseline, 1hr and 4-6hrly)**	Continuous infusion at _____ml/hr (start at 10U/kg/hr) Baseline ACT _____(normal 80-120) Keep ACT between _____and _____ Increase or decrease by 10%		

Calcium infusion	IV 10% calcium gluconate (0.5ml/kg; max 20ml) _____ml over 2 hours	
Heparin Lock	Heparin locked lumen; <5kg – 330 units in 10ml NS (33 U/ml) >5kg – 1000 units in 10 ml NS (100 U/ml)	
Blood investigations	Baseline (pre-plasmapheresis)	PT/PTT ACT (Low range) FBC ME/iCa ABG
	During plasmapheresis every hour	iCa ACT (Low range) ME Q 2 hourly/PRN
	Post plasmapheresis	PT/PTT ACT (Low range) FBC ME/iCa

Duration (min) = {Plasma volume x exchange (1 or 1.5times)} / Plasma filtration rate