INTRAVENOUS IMMUNOGLOBULIN (IVIg) ADMINISTRATION IN RENAL TRANSPLANT RECIPIENT

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**Purpose**

To provide guidance in the ordering and administration of intravenous immunoglobulin (IVIg) replacement to adult renal transplant patients of Westmead Hospital who meet criteria according to the National Blood Authority’s (NBA) “Criteria for the Clinical Use of Intravenous Immunoglobulin in Australia” (2007). It is not applicable to all other clinical populations WSLHD using IVIg.

**Scope**

This procedure applies to medical and nursing staff caring for renal transplant recipients of Westmead Hospital who require IVIg replacement therapy.

Medical officers must ensure appropriate ordering and management of IVIg’s.

Nursing staff are responsible for the safe and accurate administration and management of IVIg infusions. Nursing staff must ensure the appropriate monitoring and immediate follow-up care of patients receiving any form of immunoglobulin replacement therapy.

**Definitions**

Abbreviation and terms

<table>
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<th>IVIg</th>
<th>Intravenous Immunoglobulin</th>
<th>TE</th>
<th>Thrombotic Events</th>
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<tr>
<td>DSA</td>
<td>Donor Specific Antibody</td>
<td>PE</td>
<td>Pulmonary Embolus</td>
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<td>ABO</td>
<td>Universal blood group</td>
<td>DVT</td>
<td>Deep Vein thrombosis</td>
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<td>ABOi</td>
<td>Blood group incompatible</td>
<td>ATG</td>
<td>Anti-thymocyte globulin</td>
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<td>ACR</td>
<td>Acute Cellular rejection</td>
<td>PCR</td>
<td>Polymerase Chain Reaction</td>
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<td>ABMR</td>
<td>Antibody Mediated rejection</td>
<td>PEx</td>
<td>Plasma Exchange</td>
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<td>BK</td>
<td>Polyoma virus</td>
<td>PPE</td>
<td>Personal Protective Equipment</td>
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<tr>
<td>BKVAN</td>
<td>BK virus associated nephropathy</td>
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*Intravenous Immunoglobulin (IVIg): a fractionated blood product made from pooled human plasma. It is used in the treatment of a limited number of renal transplant conditions where immunoglobulin replacement or immune modulation therapy is indicated. IVIg is primarily used to allow transplantation that would not otherwise occur and in graft preservation for appropriately selected patients and clinical settings (Jordon et.al. 2011).*
Introduction

Patients with Renal Transplants currently account for up to 6% of IVIg internationally for various conditions. IVIg been associated with an increased incidence of thrombosis in this patient population (Huang et.al. 2011; Duronio et.al. 2007).

The mechanism of thrombosis with IVIg is not fully understood. A few theories have been proposed including transient hypercoagulability resulting from protein binding, increase in serum viscosity and elevated red blood cell aggregation (Huang et.al. 2011; ) A non-haematological hypothesis suggests that some of the other co-morbid factors associated with kidney disease are also attributable to clot formation in this population, including hyperlipidaemia, hypertension, diabetes along with personal and family history of vascular disease (Daniel et.al. 2012; Caresse et.al. 2009; Zaiden et.al. 2003). A higher osmolarity in the IVIg product itself has also been affiliated with increased thrombotic events (TE) seen post infusions (Jorden et.al. 2011)

The routine administration of hydration, aspirin and clexane along with slow infusion rates have been proposed to reduce the incidence of thrombosis in high risk patient populations (Huang et.al 2011; Isbell et.al, 2012; Zaiden et.al. 2003).
Procedure

Indications for IVIg in Renal Transplantation:


Pre-transplantation

Patients in whom antibody/antibodies are at levels that prevent transplantation

- Patients with significant DSA levels, as part of a Desensitisation regimen
- ABOi transplant recipients, as part of the ABOi protocol

Post-transplantation

Patients with

a) Biopsy proven cellular rejection unresponsive to steroids with ongoing clinical evidence of graft dysfunction

b) Biopsy proven ABMR with clinical evidence of graft dysfunction

c) Where conventional immunosuppressive therapy is contraindicated, for example

- life-threatening infections in whom conventional immunosuppressive therapy is contraindicated
- where the use of T cell depleting therapies such as thymoglobulin/ATG products or B cell depleting agents such as Rituximab are contraindicated

a) Where the patient has BKVAN diagnosed on biopsy or the BK PCR quantification levels are greater than $3 \times 10^3$ with associated graft dysfunction

b) Where patient has biopsy proven recurrence of their primary renal disease where IVIg is used in conjunction with plasma exchange
DOSAGE of IVIg

- Dosage guidelines are contained within the “Criteria for the Clinical Use of Intravenous Immunoglobulin in Australia” (2007), and are ordered through Red Cross Blood Service (see Appendix 1 or http://www.transfusion.com.au/iTransfuse/resources/forms#forms_ivig).
- IVIg product for this patient population includes the 5 & 6% concentrations and lower osmolarity formulations only.
- Immunoglobulin dose must be rounded to the nearest whole vial size to reduce the chance of product wastage.
- The dosage of IVIg is also dependent on the clinical requirements for the product (outlined below), along with if IVIg is given independently or in conjunction with Plasma Exchange (PEx) or ABO columns.

Storage

- Intravenous immunoglobulin preparations must be stored at 2 - 8°C (Refrigerate, Do not Freeze) until use (Intragam P Product Information, 2012; Kiovig 10% Product Information, 2011; Octagam CMI, 2011).
- Once removed from refrigeration, store at below 25°C and use within 3 months or as directed (Intragam P Product Information, 2012; Kiovig 10% Product Information, 2011).
- Allow to reach room temperature before administration (Intragam P Product Information, 2012).
- Do not use after expiry date (Intragam P Prod4uct Information, 2012; Kiovig 10% Product Information, 2011; Octagam CMI, 2011).
- Shelf life for some products may be restricted, always check expiry dates (Kiovig 10% Product Information, 2011).
Dosage Requirement for IVIg Administration

Pre-transplant

a) Desensitisation protocol
   - 0.5 - 1 g/kg given as one dose on day -1 pre transplant

b) ABOi protocol
   - 0.5 - 1 g/kg given as one dose on day -1 pre transplant

Post-transplant

a) Steroid resistant rejection and where convention therapy contra-indicated
   - Total of 1-2 g per kg over 6 doses given three times per week (depending on severity of graft damage on biopsy)

b) Acute ABMR
   - 0.1 to 0.5 g per kg post plasma exchange

c) Chronic ABMR
   - Total 2 g per kg over 10 doses given three times per week

d) BKVAN
   - Total 1 g per kg over 10 doses given as weekly infusions
     - ie 0.1 mg/kg/dose
Administration of IVIg and Associated Treatment Modalities

- Valid consent is required prior to the administration of any blood product, including IVIg.
- Infusion of IVIg should ideally be conducted during the day (0800 – 2000hrs). It is very rare that the infusion of IVIg is an urgent procedure requiring administration after hours. The prescribing Registrar must confirm if an after-hours infusion is necessary.
- Ensure the insertion and / or patency of any vascular access device prior to removing immunoglobulin dose from refrigeration.
- Pre-infusion hydration given.
- Pre-infusion anti-coagulation given.
- Dose is administered via a set infusion rate outlined below.
- Patients receiving blood products should have hospital ID band to provide appropriate identity check
- Two members of staff must undertake the identity check of the patient and IVIg at the patient’s bedside/chairside immediately prior to administration (as per Blood Administration Policy, 2007).
- The staff performing the identity check must be medical officers, registered nurses or registered midwives. Both individuals who complete the checking procedure must also sign the relevant documentation.
- The person spiking/administering the product must be one of the two who performed the bedside check, and must comply with the guidelines surrounding the administration of blood products.
- Patients receiving IVIg must be monitored for the occurrence of adverse reactions (see Educational Notes).

Infusion rate

Infusion rate = 1ml/kg/hr,
this slow rate is required for the duration of the infusion (Huang et al, 2009)
Pre-IVIg Infusion Requirements

- IV hydration: 500mL 0.9% sodium chloride (unless otherwise indicated by medical officer) over 1 hr.
- Anti-coagulation: Enoxaparin (Clexane) at a dose of 1mg/kg. (If enoxaparin contra-indicated then 5,000 units of intravenous heparin can be administered).

Equipment

- 0.9% sodium chloride 1 litre
- Immunoglobulin dose
- Anti-coagulant dose
- Infusion pump
- Standard IV infusion set with air inlet
- Patent vascular access (this may be either peripheral or central)
- Personal Protective Equipment (PPE)

Observations

- Observations should be taken and recorded as per Blood Administration policy and manufacturer’s guidelines. At least, record vital signs (temperature, pulse, blood pressure and respiratory rate):
  - Baseline prior to infusion commencing
  - After the first 15mins of infusion
  - Then hourly until completion
  - At the completion of the infusion
- If the patient’s condition deteriorates, more frequent monitoring and recording of vital signs may be necessary (Between The Flags Clinical Emergency Response Policy Westmead Hospital, 2011).
- If patient is diabetic, BSL should be taken prior to infusion commencing and at the completion of the infusion due to the sugar content of the preparation
Risk Rating

Medium.
Risk of Non-compliance: Patient may experience adverse reaction and/or discomfort from inappropriately administered intravenous immunoglobulin.
Unsafe administration of intravenous immunoglobulin and/or suboptimal management of patients receiving intravenous immunoglobulin may lead to increased morbidity and mortality of patients.

Implementation Plan

- This protocol is only approved for the clinical indications mentioned above, deviation of protocol requires review by the haematology team
- Implemented in accordance with current ICPMR (Haematology & Blood Bank) practices
- Available via Renal Shared Drive and Protocol Folders in A6 Westmead Hospital
- Education to medical and nursing staff conducted as necessary
**Education Notes**

- Intravenous immunoglobulin is a blood product. Administration and monitoring procedures must follow those contained in the Blood Product administration policy of WSLHD and according to guidelines published by ANZSBT and Australian Red Cross Blood Service.

- As with any blood product or medication, there is a chance that the patient may develop an adverse reaction upon administration. This can range from very mild reactions to serious and life-threatening reactions. A list of adverse reactions for each product may be found in the corresponding product information sheet *(Intragam P Product Information, 2012; Kiovig 10% Product Information, 2011; Octagam CMI, 2011)*.

- In the event of a serious or life-threatening adverse reaction, such as anaphylaxis, cease the infusion and initiate a clinical emergency response call as appropriate for your facility, and keep vascular access patent. *Do not recommence infusion until reviewed by Medical Officer* *(ANZSBT Guidelines, 2011; Between The Flags Clinical Emergency Response Policy Westmead Hospital, 2011; Blood Administration Policy, 2007)*.
References and Related Policies

- Pierce LR, Jain N. Risks associated with the use of intravenous immunoglobulin. Transfusion Medicine Rev 2003; 17: 241


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