South Australian Perinatal Practice Guidelines

Intravenous Immunoglobulin (IVIg) infusion

Intravenous immunoglobulin (IVIg)

IntragamP®, Kiovig 10 % and Octagam® 5 % and 10 %

- IVIg is Intravenous Immunoglobulin
- The National Blood Authority 'Criteria for the clinical use of IVIg' specifies the funded use of IVIg in Australia
- Intragam P®, CSL Biotherapies, is made from non-remunerated Australian donor plasma. Kiovig 10 %, Baxter, Octagam® 5 % and Octagam® 10 %, Octapharma, are manufactured from European and USA remunerated and non-remunerated donor plasma
- All products contain at least 98 % IgG with traces of IgA and IgM. The distribution of IgG subclasses is similar to that found in normal serum
- Intragam P® is made by chromatographic fractionation of large pools of human plasma. The protein has not been chemically or enzymatically modified. The manufacture process has two dedicated viral reduction steps. It is stabilised in maltose which may create false high blood glucose readings in some bedside glucometers
- Kiovig 10 % is made by cold ethanol fractionation, ion exchange chromatography and ultrafiltration from large pools of human plasma. The manufacture process has three dedicated viral reduction steps. It is stabilised in glycine
- Octagam® 5 % and Octagam® 10 % are made by cold ethanol fractionation of large pools of human plasma. The protein has not been chemically or enzymatically modified. The manufacture process has two dedicated viral reduction steps. It is stabilised in maltose which may create false high blood glucose readings in some bedside glucometers.
- Stringent controls are applied to the selection of blood donors; however, virus removal and inactivation procedures in the production process are of reduced value against non-enveloped viruses
- Vaccination for women in receipt of human blood or plasma products should be considered where appropriate
- Women who require IVIg should be cared for in tertiary institutions

Literature review

- Controlled clinical trials have not established the safety of IVIg for use in pregnancy and lactation. Long lasting clinical experience indicates no harmful effects on the course of the pregnancy, the fetus or the neonate
- Immunoglobulins are excreted into breast milk and may contribute to the transfer of protective antibodies to the neonate

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Indications

Replacement therapy in immune disorders

- Primary immune deficiency syndromes for which replacement of IgG is intended

Immunomodulation therapy

- May also be of benefit as an alternate treatment for idiopathic thrombocytopenic purpura
- Feto-maternal / neonatal alloimmune thrombocytopaenia (not suitable for rhesus isoimmunisation)

Staphylococcus and Streptococcus toxic shock syndrome (TSS)

- IVIg may be useful where there is failure to achieve rapid improvement with fluid resuscitation and inotropes, in addition to surgical intervention, antibiotic therapy and other supportive measures (NBA 2007)
- (for further information on toxic shock syndrome, refer to the PPG 'Sepsis in pregnancy')

For further information refer to the 'Criteria for the clinical use of intravenous immunoglobulin in Australia' Dec. 2007 (Available from URL: www.nba.gov.au)

Contraindications

- Women with a history of an anaphylactic reaction to a human immunoglobulin preparation
- Individuals with selective IgA deficiency who have IgA antibodies (may provoke anaphylaxis due to trace amounts of IgA in IVIg. The lowest IgA containing IVIg should be selected. Intragam P® reports lower IgA than Kiovig 10 % or Octagam® 5 % or 10 %

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Precautions

- Rarely may cause a precipitous fall in blood pressure and a clinical picture of anaphylaxis
- Aseptic meningitis syndrome (AMS) is an infrequent complication. Exclude by thorough neurological examination including CSF studies (rules out other causes of meningitis)
- The risk of red cell sensitisation following high dose IVIg infusion may cause cross matching difficulties and transient haemolytic anaemia
- Renal function should be monitored in women at risk of acute renal failure
- The following women may be at increased risk of renal dysfunction and acute renal failure:
  - Pre-existing renal insufficiency
  - Diabetes mellitus
  - Fluid volume depletion
  - Sepsis and paraproteinaemia
  - Those taking concomitant nephrotoxic drugs
- **The maltose present in Intragam P® and Octagam® 5 % and 10 % may result in falsely elevated capillary blood glucose levels with some types of glucose meters (e.g. acutrend advantage). Clinicians are advised that if this measurement is used to guide treatment, hypoglycaemia may occur**

Dosage and administration

- Women should be adequately hydrated before initiation of an IVIg infusion
- Administered intravenously, 100 % of the infused IgG antibodies are immediately available in the recipient's circulation
- Prolonged administration over 6 hours using large doses (> 400 mg / kilogram) may result in thrombophlebitis at the infusion site
- Stickers (indicating lot numbers) from the IVIg bottle should be placed in the case notes to facilitate the retrace of batch numbers in the event of product recall

Dosage

- Do not exceed the recommended dose
- Reactions tend to be related to the infusion rate and are most likely to occur during the first hour
- Monitor vital signs and general status throughout the infusion

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Administration

- Adrenaline, oxygen, antihistamines and steroids should be available for immediate use during administration to treat true hypersensitivity reactions
- Intragam P® is stored refrigerated at 2°C to 8°C (not frozen), and once removed from refrigeration, can be stored below 25°C and used within 3 months
- Kiovig 10 % is stored refrigerated at 2°C to 8°C (not frozen), and once removed from refrigeration, can be stored below 25°C and used within 12 months if removed from refrigeration in the first 24 months
- Octagam® 5 % may be stored below 25°C for 2 years
- Octagam® 10 % is stored refrigerated at 2°C to 8°C (not frozen), and once removed from refrigeration, can be stored below 25°C and used within 3 months
- Do not use a product that is turbid or contains sediment – return unopened to blood transfusion service
- Use immediately after opening the bottle (no antimicrobial agent)
- Discard unused portions and do not use if the solution has been frozen
- All IVIg products are infused undiluted
- Use a dedicated intravenous line and administer at room temperature
- Infuse through an infusion pump
- The first time a woman receives IVIg; administration is started slowly and increased steadily if no adverse events

Infusion / observation instructions

Infusion instructions

- Use ideal body weight (60 kg) to calculate infusion rates in obese women
- All IVIg products may be administered through any standard intravenous infusion set
- Remove the dust cover from the top of the bottle
- Swab the rubber stopper with appropriate antiseptic wipe and allow to dry
- Use an intravenous line with a vent or a vented spike adaptor
- Insert the giving set into the central indentation of the stopper
- Invert the bottle and attach the hanger to a support approximately one metre above the woman
- Prime the line and attach to the intravenous site

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Administration of Intragam P® Adult

NOTE: Incremental rates for the Adult infusion of Intragam P® are in mL per hour (not weight based).

- Commence at 60 mL per hour (1 mL per minute) for 15 minutes - (15 mL)
- Double infusion rate every 15 minutes to a maximum of 240 mL per hour (4 mL per minute) until infusion is complete
- A more conservative maximum rate should be considered for women with the following risk factors: obesity, diabetes, cardiac disease, renal failure, arterial or venous thromboembolic events or hyperviscosity (BloodSafe 2012)
- If headache or other minor symptoms occur, notify medical officer, cease infusion for 10 minutes, then recommence at a slower rate i.e. 180 mL per hour

Administration of Kiovig 10%

- Commence at 0.5 mL per kilogram per hour (30 mL per hour for a 60 kg woman) for the first 30 minutes
- Increase the infusion rate every 30 minutes as below with a maximum of 300 mL per hour until infusion is complete (BloodSafe 2012)
  - 0.5 mL per kilogram per hour (30 mL per hour for a 60 kg woman)
  - 1.0 mL per kilogram per hour (60 mL per hour for a 60 kg woman)
  - 2.0 mL per kilogram per hour (120 mL per hour for a 60 kg woman)
  - 3.0 mL per kilogram per hour (180 mL per hour for a 60 kg woman)
  - 4.0 mL per kilogram per hour (240 mL per hour for a 60 kg woman)
  - 5.0 mL per kilogram per hour (300 mL per hour for a 60 kg woman)
- A more conservative maximum rate of 200 mL per hour is recommended for women with the following risk factors: obesity, diabetes, cardiac disease, renal failure, arterial or venous thromboembolic events or hyperviscosity (BloodSafe 2012)
- If headache or other minor symptoms occur, notify medical officer, cease infusion for 10 minutes, then recommence at a slower rate

Administration of Octagam® 5%

- Commence at 1 mL per kilogram per hour (60 mL per hour for a 60 kg woman) for the first 30 minutes
- Increase the infusion rate every 30 minutes as below with a maximum of 300 mL per hour until infusion is complete (BloodSafe 2012)
  - 0.5 mL per kilogram per hour (30 mL per hour for a 60 kg woman)
  - 1.0 mL per kilogram per hour (60 mL per hour for a 60 kg woman)
  - 2.0 mL per kilogram per hour (120 mL per hour for a 60 kg woman)
  - 3.0 mL per kilogram per hour (180 mL per hour for a 60 kg woman)
  - 4.0 mL per kilogram per hour (240 mL per hour for a 60 kg woman)
  - 5.0 mL per kilogram per hour (300 mL per hour for a 60 kg woman with a maximum rate of 480 mL per hour)
- A more conservative maximum rate of 300 mL per hour is recommended for women with the following risk factors: obesity, diabetes, cardiac disease, renal

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failure, arterial or venous thromboembolic events or hyperviscosity (BloodSafe 2012)

- If headache or other minor symptoms occur, notify medical officer, cease infusion for 10 minutes, then recommence at a slower rate

Administration of Octagam® 10%

- Commence at a rate between 0.5 mL per kilogram per hour (30 mL per hour for a 60 kg woman) for the first 30 minutes
- Increase the infusion rate every 30 minutes as below with a maximum of 300 mL per hour until infusion is complete (BloodSafe 2012)
  - 0.5 mL per kilogram per hour (30 mL per hour for a 60 kg woman)
  - 1.0 mL per kilogram per hour (60 mL per hour for a 60 kg woman)
  - 2.0 mL per kilogram per hour (120 mL per hour for a 60 kg woman)
  - 3.0 mL per kilogram per hour (180 mL per hour for a 60 kg woman)
  - 4.0 mL per kilogram per hour (240 mL per hour for a 60 kg woman)
  - 5.0 mL per kilogram per hour (300 mL per hour for a 60 kg woman)
- A more conservative maximum rate of 200 mL per hour is recommended for women with the following risk factors: obesity, diabetes, cardiac disease, renal failure, arterial or venous thromboembolic events or hyperviscosity (BloodSafe 2012)
- If headache or other minor symptoms occur, notify medical officer, cease infusion for 10 minutes, then recommence at a slower rate

Observations

- Monitor vital signs before the infusion, then 15 minutely for 30 minutes, then hourly until infusion completed
- Continuous external fetal heart rate monitoring is not required unless there are other specific indications. Obtain fetal heart on admission and before discharge
- Observe woman for 30 minutes after completion
- Observe for 1 hour after completion if:
  - First IVIg infusion
  - Change in IVIg product
  - Long interval since the last infusion
  - There is a significant deterioration in the woman's health
  - A reaction to the current or a previous infusion (BloodSafe 2012)

Side effects

- Observe for nausea, vomiting, chest pain, rigors or aching legs (may occur up to 24 hours after infusion).
- 5 to 15 % of people receiving IVIg develop a mild or moderate headache and a mild loss of appetite for about 24 hours

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Discharge planning

- Explain that the above side effects may occur up to 24 hours
- Educate the woman to return to the hospital if signs of AMS develop e.g.
  - Severe headache
  - Nuchal rigidity
  - Drowsiness
  - Fever
  - Photophobia
  - Painful eye movements
  - Nausea and vomiting
- Discharge following medical review

References

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Useful references

Flippin blood – A Bloodsafe flip chart to help make transfusion straight forward
http://www.health.sa.gov.au/bloodsafe/Portals/0/flippn'bloodchartSept06.pdf

BloodSafe – transfusion practice
http://www.health.sa.gov.au/bloodsafe/Default.aspx?tabid=83

Criteria for the clinical use of intravenous immunoglobulin in Australia
http://www.nba.gov.au/ivig/pdf/criteria.pdf

Abbreviations

AMS	Aseptic meningitis syndrome
APPG	Australian Prescription Products Guide
ARCBS	Australian Red Cross Blood Service
C	Celsius
CSF	Cerebrospinal fluid
CSL	Commonwealth Serum Laboratories
e.g.	For example
IV	Intravenous
IVIg	Intravenous immunoglobulin
mg	Milligram(s)
mL	Millilitre(s)
mm Hg	Millimetres of mercury
NZBS	New Zealand Blood Service
%	Percent
â	Registered trademark
TGA	Therapeutic Goods Administration

Version control and change history

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