Identification and management of anaemia In chronic kidney disease patients

INDEX:

SUMMARY

The current haemoglobin (Hb) range will now be set at **10 to 12 g/dL** (1,2). Anaemia is a known risk factor for the development of cardiovascular co-morbidities in CKD patients as well as a reduction in quality of life (3,4).

All possible causes for anaemia should be identified prior to commencing any ESA therapy (1, 3).

The lowest dose ESA will be used for each patient to achieve recommended Hb targets, improve quality of life and prevent the need for blood transfusions (5, 6).

Correction and maintenance of functional iron stores to optimal levels will be an effective treatment for CKD patients with low Hb levels prior to and during ESA therapy (1, 3, 4).

Haemoglobin, iron stores and ESA dosing for patients with CKD will be maintained at optimal levels to provide for an improved quality of life and a decrease in adverse symptoms (3,4).

Nursing staff will check monthly blood results and monitor patients for adverse signs and symptoms, organizing a review of ESA dosing and iron requirements with the Nephrologist as necessary to provide for optimal patient outcomes (4).

Aiming for a Hb target of > 130 g/dL can lead to negative outcomes for all patients with CKD, such as hypertension, MI, stroke and vascular access blockages (1, 3, 7, 8).

1. WHAT OTHER GUIDELINES SAY:

CARI GUIDELINES: (2006)

- The targeting of haemoglobin concentrations above 130 g/L has been associated with an increased mortality in chronic kidney disease (CKD) patients (dialysis and pre-dialysis) and is therefore currently considered inadvisable. (Level I evidence)
- Achieve and maintain haemoglobin above 110 g/L (Level III and IV)
- Maintain serum ferritin 200 – 500 ug/L and Tsats 30 – 40% during ESA therapy
- Monitor iron levels 3 monthly for patients on ESA who have attained target Hb
- Monitor iron levels monthly on commencement and during periods of increased ESA dosing
- Delay monitoring for at least 2 weeks after iron dosing of > 200 mg
- The haemoglobin concentration should be checked at least every 2 months and iron stores at least every 3 months. Vitamin B12 and folate levels should be checked at least every 12 months. (Opinion)
- IV iron may be needed at initiation of ESA
- If serum ferritin is > 500 µg/L (or TSAT > 40%), withhold IV iron for up to 3 months. When serum ferritin declines to < 500 µg/L (or TSAT < 40%), IV iron can be resumed at a reduced dose/frequency
- http://www.cari.org.au

KDOQI CLINCIAL PRACTICE GUIDELINES:

- All other potential causes for low Hb levels other than EPO deficiency should be identified or excluded
- 2.1.2 In the opinion of the Work Group, in dialysis and nondialysis patients with CKD receiving ESA therapy, the selected Hb target should generally be in the range of 11.0 to 12.0 g/dL. (Clinical Practice RECOMMENDATION)
- 2.1.3 In dialysis and nondialysis patients with CKD receiving ESA therapy, the Hb target should not be greater than 13.0 g/dL. (Clinical Practice GUIDELINE - MODERATELY STRONG EVIDENCE)
- http://www.kidney.org/kidneyDisease

KDIGO announces Anaemia Guideline update:

- "An updated anemia guideline is considered necessary in light of new study results, particularly the data from “Trial to Reduce Cardiovascular Events with Aranesp Therapy” (TREAT) which was made public in November. The process will be accelerated to publish the guideline in a year rather than two years to ensure that practitioners and patients benefit from new knowledge as soon as possible,” said Kai-Uwe Eckardt, MD, Head of Nephrology and Hypertension at the University of Erlangen-Nuremberg in Germany and Co-Chair of KDIGO
- http://www.kdigo.org

EUROPEAN RENAL BEST PRACTICE GUIDELINES: (10,17)

- **Haemoglobin target:** In 2004, EBPG suggested an Hb target of ≥11 g/dl; values of >14 g/dl were considered undesirable in general, and the limit for patients with cardiovascular disease was set at 12 g/dl.
- **Targets for iron therapy:** Traditionally, the most widely used iron tests are serum ferritin and transferrin saturation (TSAT) levels. In 2004, EBPG recommended lower limits of ferritin and TSAT of, respectively, 100 ng/ml and 20%, with target ranges of respectively 200–500 ng/ml and 30–50%.
- If serum ferritin levels are > 500 ng/mL, iron administration should be discouraged.
- http://ndt.oxfordjournals.org/cgi/reprint/24/2/348

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UK RENAL ASSOCIATION: (1)

- Patients with CKD should achieve an outcome distribution of haemoglobin of 10.5 – 12.5 g/dl
- Adjustments to ESA doses should be considered when Hb is < 11 or > 12 g/dl in order that the population distribution has the maximum proportion of patients in the range 10.5 – 12.5 as is possible

CANADIAN SOCIETY OF NEPHROLOGY (CSN) 1999 (1)

- The target haemoglobin during epoetin therapy is advised to be between 110 and 120 g/L for both men and women
- It is suggested that epoetin be used before and after initiation of dialysis

2. CAUSES, SYMPTOMS AND BENEFITS OF ANAEMIA CORRECTION:

Causes	Symptoms	Benefits
Insufficient production of EPO	Loss of well-being	Improved quality of life
Iron deficiency	Shortness of breath on exertion	Regression of LVH and CVD
Reduced half life of RBC	Tiredness, increased fatigue, lack of energy	Increased energy levels
Insufficient B12 and folate	Exercise intolerance	Increased exercise capacity
Chronic blood loss (blood tests, dialysis process, low platelet counts)	Sleep disorders	Improved sleeping patterns
Hemolysis due to dialysis process	Impaired cognitive functioning	Improved cognitive functioning
Infection/inflammation	Decreased sexual drive	Improved sexual functioning
Haemoglobinopathies (eg sickle cell anaemia)	Decreased immunity	Immune responsiveness
Elevated PTH (leading to osteitis fibros)	Pallor (lips, palms and tongue)	Improved haemostasis
Hyperphosphateamia		Menstrual regularity (women)
Malnutrition		Reduction in hospital admissions
Medication use		Reduction in morbidity and mortality
Liver disease		

3. RECOMBINANT HUMAN ERYTHROPOIETIN (EPO) THERAPY:

Indications for use: (4)

- Hb <100 g/L
- No other identifiable causes

Target Hb: (5)

- 100 to 120 g/L
    - Check monthly when in range

Dosage: (3)

- Epoeitin
    - Initial dose: 80 – 120 IU/kg/week in divided doses
    - Maximum dose: 900 IU/kg/week
- Darbepoetin alfa
    - Initial dose: 0.45ug/kg/week in a single dose

Route of administration: (3, 16)

- Haemodialysis patients:
    - Given as either sub-cut or intravenous injection
- Predialysis and PD patients:
    - Given as a sub-cut injection, with rotation of site

Response to ESA therapy: (1, 2)

- **Prior to commencing treatment:**
    - Check FBC
    - Iron studies
    - B12 and folate levels
    - Check CRP (indication of infection and/or inflammation)
- **Once treatment has been commenced: (1, 2)**
    - Monitor BP
    - Check Hb 2nd weekly until Hb within range
    - Monitor iron studies monthly until Hb has stabilized.

3.1 INADEQUATE RESPONSE TO EPO THERAPY:

- In patients with inadequate response to EPO, possible causes should be investigated (12, 14)

- **Possible causes:**
    1. Absolute or Functional Iron Deficiency
    2. Insufficient levels of B12 and folate
    3. Infection/inflammation (i) p 368
        a. Including access infection and auto-immune diseases
        b. Up to 53% of patients can have elevated levels of serum CRP
    4. Chronic blood losses
        a. Retention of blood in lines and dialyser
        b. Blood sampling for laboratory testing
        c. Accidental bleeding from access and surgical blood losses
        d. Occult gastrointestinal bleeding
    5. Inadequate dialysis
    6. Malnutrition, low albumin and poor absorption of oral iron
    7. Elevated PTH and hyperphosphatemia
        a. Associated with bone marrow fibrosis
    8. Aluminium toxicity
    9. Haemoglobinopathies
    10. Multiple myeloma or other malignancies
    11. Hemolysis
    12. Alcohol consumption

3.2 COMPLICATIONS OF EPO THERAPY: (12, 16)

1. Worsening of hypertension:
    a. 33% of patients will need to increase antihypertensive medication
    b. Not found in anaemic patients without renal disease who are treated with EPO
    c. Risk factors
        i. pre-existing hypertension
        ii. rapid increase in hematocrit
    d. Possible causes:
        i. reversal of hypoxic vasodilatation as hematocrit rises
        ii. increased blood viscosity
        iii. increased cardiac output

2. Seizures:
    a. Small risk associated with periods of rapidly rising hematocrit

3. Fistula/graft thrombosis:
    a. No conclusive evidence
    b. Risk associated with increased blood viscosity

4. Underdialysis and decreased Kt/V:
    a. Associated with increased clotting of dialyser
    b. Reduced proportion of plasma to red cell volume

5. Phosphorus balance:
    a. Associated with an improvement in appetite and dietary intake in combination with reduced dialyser clearance

6. Flu-like symptoms immediately following injections
    a. Can last up to a few hours to weeks after injection

4. Evidence to support a Hb range of 10 to 12 g/dL:

- Hb range of 10 to 12 g/dL may be a more appropriate, affordable and safer target than the narrow Hb range of 11-12 g/dL (5)

- Scientific evidence supports a target Hb level of > 10 to 11 g/dL in all CKD patients with no survival benefits at higher levels of anaemia correction (3)

- The Normal Hematocrit Study and the CHOIR trial were consistent with the finding that haemoglobin-concentration targets > 13 g/dL and the ESA dosing to achieve them can be harmful (7, 8)

- TREAT showed no evidence of benefit and a trend toward overall harm in the higher haemoglobin target group receiving aranesp (7, 8)

- CHOIR and TREAT raised major concerns regarding the use of ESAs to increase Hb targets above a level needed to avert the use of blood transfusions (7, 8)

- More conservative targets, well below 12 g/dL, should be considered and evaluated (7)

- The FDA and Amgen (the manufacturer of Aranesp, Epogen and Procrit) have issued a new warning: (6)
    - Avoid serious cardiovascular and thromboemolic events by using the lowest dose of ESA that will gradually raise the Hb to the lowest level which will avoid the need for a blood transfusion
    - ESAs increase the risk for death and serious cardiovascular events when the target Hb is greater than 12 g/dL
    - All ESAs have the same mechanism of action and therefore the above concerns apply to all ESAs

- Reaching and maintaining a target Hb level of patients with renal failure is challenging – only 48% met Amgen's target range (10 to 12 g/dL) and only 40.7% met the KDOQI recommended Hb level (11 to 12 g/dL) – Annual Report of the United States Renal Data System (USRDS) (2008) (9)

- An individual's demographic, disease characteristics and co-morbidities must be important considerations in determining target Hb (10)

5. MONITORING OF IRON STATUS AND IRON SUPPLEMENTATION IN PATIENTS WITH CKD:

Markers used to monitor Iron status: (14)

1. Serum ferritin
   - 200 to 800 ng/ml (recommended range)
   - Correlates with storage iron in liver, spleen and bone marrow reticuloendothelial cells
2. Transferrin saturation (TSAT)
   - 20 to 50 % (recommended range)
   - = serum iron (ug/dl) / TIBC (ug/dl) x 100
   - Correlates with iron readily available for erythropoiesis
3. CHr (Reticulocyte haemoglobin content) (i) p 368
   - 25.9 – 33.9 pg (normal range)
   - Correlates with a real-time estimate of iron availability for haemoglobin production in the bone marrow
   - Levels are not elevated during inflammation
   - Greater sensitivity and specificity than classic iron markers

Frequency for monitoring Iron Studies: (1,2)

- Monthly:
  - during initiation or adjustment of EPO therapy
  - after completion of course of IV iron
  - during periods of iron overload
- 3rd monthly:
  - all patients with stable adequate iron stores

Indications for Iron deficiency: (2)

1. Initial serum ferritin level < 200 ug/L **
2. Initial Transferrin saturation < 20%
3. More than 10% hypochromic erythrocytes (individual cell Hgb < 28 g/dL)

5.1 CONTRA-INDICATIONS FOR IV IRON SUPPLEMENTATION: (12, 14)

1. Iron overload
   - Ferritin > 800 ng/ml or TSAT > 50%
2. Known allergies to Ferrosig and/or Venofer

5.2 INDICATIONS FOR IV IRON INFUSION:

1. Intolerance to oral iron
2. Worsening of iron deficiency or suboptimal response to EPO despite oral iron supplementation

5.3 IV IRON INFUSIONS AVAILABLE:

IV Iron solutions available: (Check with Pharmacy for availability and suitability)

1. Iron polymaltose (Ferrosig):
    a. Incidence of adverse reaction to Ferrosig is lower than iron dextran
2. Venofer:
    a. Available for patients who have had a previous allergic reaction to Ferrosig

5.4 ADVERSE REACTIONS TO IV IRON INFUSION: (12)

- Anaphylaxis-like reactions usually occur within a few minutes after the commencement of an infusion
- A Medical Officer needs to be advised prior to the commencement of the first infusion
- There must be immediate access to the medications required for the treatment of anaphylaxis in the rare event that it may occur

A. Immediate reactions:

a. Anaphylaxis: dyspnoea, faintness, hypotension, loss of consciousness
b. Headache
c. Nausea and vomiting
d. Joint and muscle pain
e. Dizziness
f. Flushing
g. Sweating
h. Rash, including urticaria

If any of the above signs or symptoms develop, STOP INFUSION IMMEDIATELY and call for medical assistance (Pace 2):

Treatment of anaphylaxis:

1. Lie patient flat and raise their feet

2. Administer 100 % oxygen via mask

3. Administer fluid including gelofusine IV to maintain systolic BP to 100 mg Hg

4. Medical Officer to give adrenaline (1:1000) immediately 0.5 ml subcut (repeat at 5 to 15 minute intervals if necessary) followed by hydrocortisone 200 mg IV and diphenhydramine 50 mg IV

5. Commence CPR in the event of a respiratory or cardiac arrest

B. Delayed reactions:

a. Dizziness
b. Myalgia and arthralgia
c. Stiffness in arms, leg or face
d. Chest and back pain
e. Chills and fever
f. Rash, including urticaria
g. Generalised lymphadenopathy

6. RECOMMENDED DOSING SCHEDULES FOR IRON SUPPLEMENTATION:

THERE ARE TWO FORMS OF IRON DEFICIENCY: (2, 3, 14)

6.1 PATIENTS WITH ABSOLUTE IRON DEFICIENCY:

[Ferritin < 200 ng/ml and TSAT < 20%]

- **(Regime A)**

[Ferritin < 200 ng/ml and TSAT 20 – 50%]

- **(Regime B)**

6.2 PATIENTS WITH FUNCTIONAL IRON DEFICIENCY:

[Ferritin within normal range (200 – 800 ng/ml) and TSAT < 20%]

- **(Regime C)**

Treatment for Iron Deficiency:

- IV iron 100 mg each dialysis session for 10 consecutive sessions unless contraindicated
- Check Fe studies 1 month after completion of course
- Once optimal iron parameters are achieved, titrate IV iron to a monthly dose

Initial infusion:

- Renal Team/RMO needs to be advised prior to the first infusion
- Dilute 100mg IV iron in 100 mls 0.9% normal saline and infuse via an infusion control device at a rate of 15 mls/hr for the first 30 minutes (rate 15mls/hr, volume 7.5mls)
- In the absence of any reaction, increase pump speed to 120 mls/hr

Subsequent infusions:

- Draw up 100 mg IV iron into a 20 ml syringe and dilute to a volume of 10 mls with 0.9% normal saline
- Infuse via the heparin pump on the haemodialysis machine over the last 60 minutes of treatment
- Alternatively, draw up 100 mg IV iron and dilute to a volume of 5 mls with 0.9% normal saline and bolus over 5 minutes

REPEAT IRON STUDIES 1 MONTH AFTER 1ST COURSE OF IRON:

- **If Ferritin still < 200 ng/ml and TSAT still < 20%**
  - Administer 2nd course of IV iron as above

- **Repeat Iron Studies 1 month after 2nd course of iron:**

- **If Ferritin remains < 200 ng/ml and TSAT remains < 20%**

  - Revert to monthly iron until review by Nephrologist
  - Advise Nephrologist of non-response to iron in clinic letter and initiate review of possible causes

- **After a 2nd course of iron:**

- **If Ferritin 200 – 800 and TSAT still < 20%**
  - **(Regime F)**
  - Revert to monthly iron until review by Nephrologist

- **If Hb > 120 g/L and Ferritin 100 – 200 ng/ml with TSAT > 20%**
  - **(Regime G)**
  - Revert to monthly iron until review by Nephrologist

6.3 IN PATIENTS WHO ARE IRON REPLETE: (2, 3)

[**Ferritin 200 to 800 ng/ml and TSAT 20 to 50%]**

- **(Regime E)**
- Monthly maintenance IV iron 100 mg unless contraindicated

6.4 IN PATIENTS WITH IRON OVERLOAD: (2, 3)

[Ferritin > 800 ng/ml or TSAT > 50%]

- **(Regime D)**
- Withhold iron for up to 3 months
- Check Fe studies monthly
- Once Ferritin < 500 ng/ml OR TSAT < 40 %
  - Recommence monthly iron

7. HAEMODIALYSIS NURSE INITIATED IV IRON REPLACEMENT CHART:

<table>
<tr><th>Regime</th><th>Iron Studies Result</th><th>IV Iron</th><th>Regime</th><th>Iron Studies Result</th><th>IV Iron</th></tr>
<tr><td>A</td><td>Ferritin < 200ng/ml
and
TSAT < 20%</td><td>Iron 100mg for 10 sessions (max 2 courses)
Retest Iron Studies 1 month post course</td><td>F</td><td>If, after 2 courses of iron Ferritin 200 – 800 ng/ml
and
TSAT still < 20%</td><td>Revert to monthly maintenance dose & monitor Fe studies monthly until review by Nephrologist at next clinic</td></tr>
<tr><td>B</td><td>Ferritin < 200ng/ml
and
TSAT 20% - 50%</td><td>Iron 100mg for 10 sessions (max 2 courses)
Retest Iron Studies 1 month post course</td><td>G</td><td>If Hb > 120 g/L,
Ferritin 100 – 200 ng/ml
and
TSAT > 20 %</td><td>Revert to monthly maintenance dose & monitor Fe studies monthly until review by Nephrologist at next clinic</td></tr>
<tr><td>C</td><td>Ferritin 200 – 800 ng/ml
and
TSAT < 20%</td><td>Iron 100mg for 10 sessions (max 2 courses)
Retest Iron Studies 1 month post course</td><td colspan="3" rowspan="3">Target Hb:
<u>Aim for 100-120 g/L for all patients</u>

If Hb > 120 g/L withhold ESA unless otherwise advised by Nephrologist

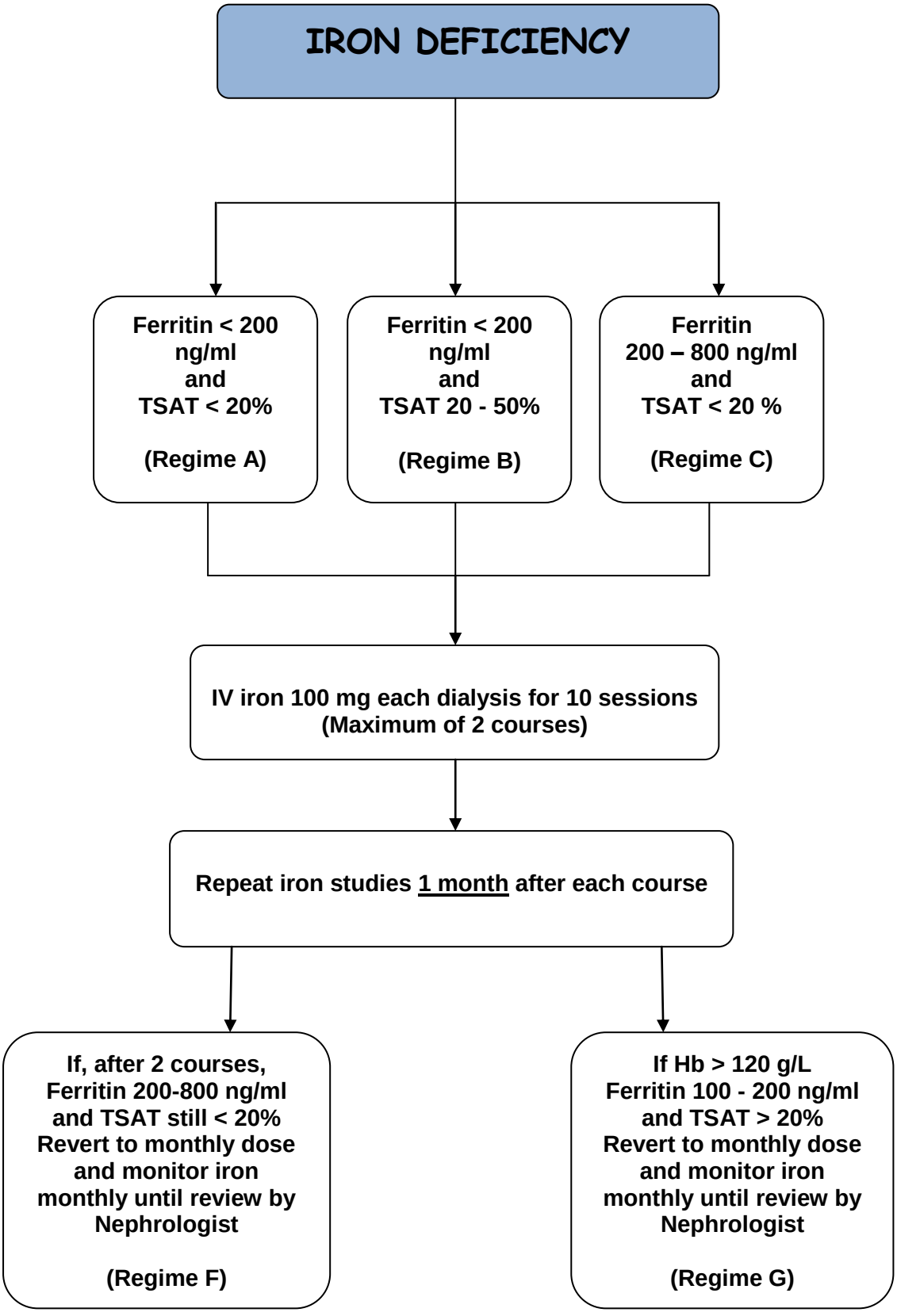
➢ Note Hb and date withheld on ESA medication chart
➢ Check Hb in 2 weeks (place note in diary)
➢ Restart ESA at a reduced dose or frequency when Hb < or = to 120 g/L
➢ <u>Always recheck Hb 2 weeks after ceasing, commencing or changing a dose of ESA</u> (place note in diary)
➢ PN to identify Hb fluctuations in next Clinic letter
➢ Doctor to review ESA and Fe Regime at next Clinic appt
➢ Once Hb within range, check Hb monthly
➢ Do not withhold monthly Fe unless Hb > 130 g/L

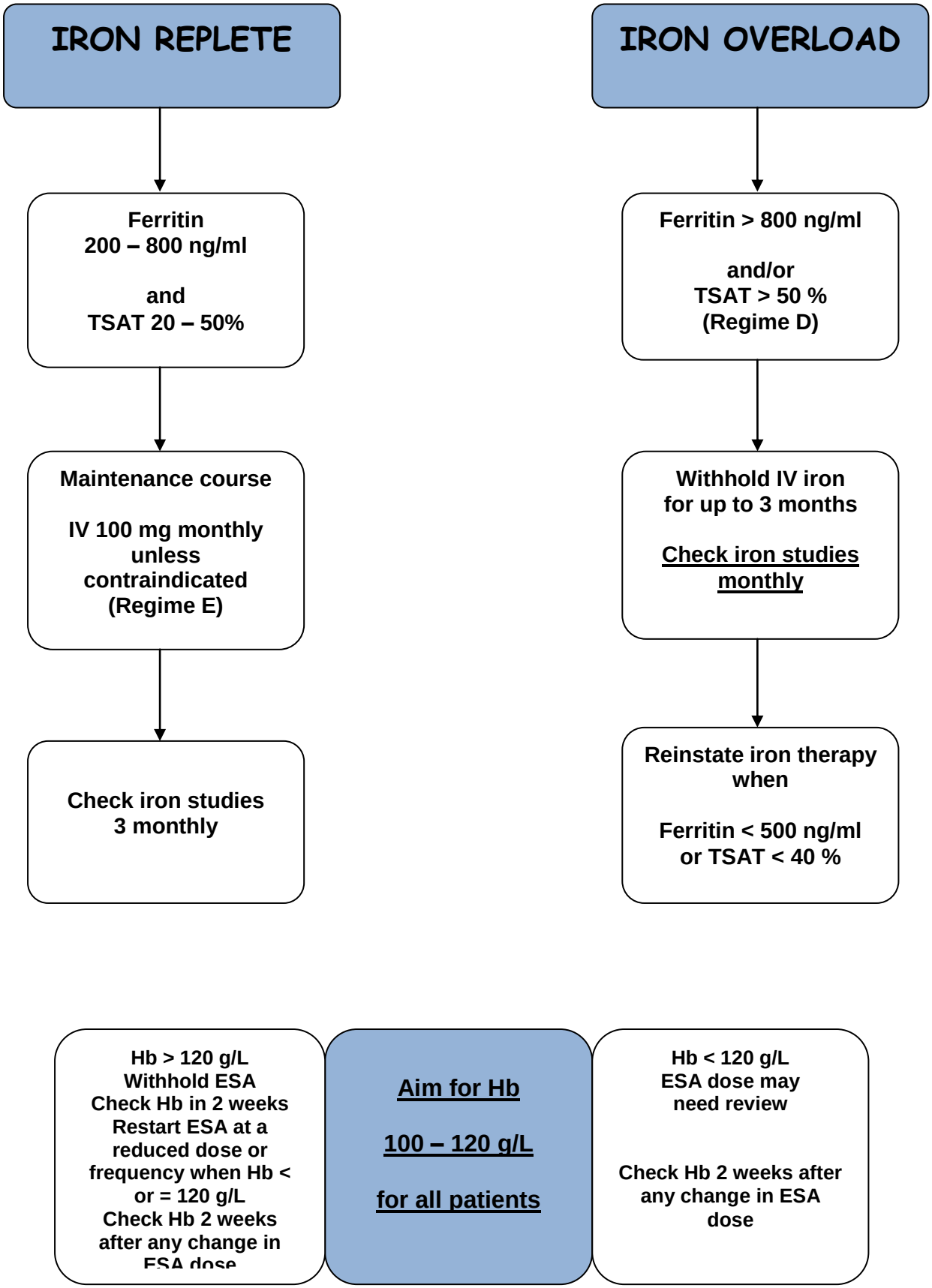
(December 2010)</td></tr>
<tr><td>D</td><td>Ferritin > 800 ng/ml

<u>OR</u>

TSAT > 50%</td><td>Withhold Iron for up to 3 months.
<u>Check Fe studies monthly</u>.
Reinstate Fe Regime when
Ferritin < 500ng/ml <u>OR</u>
TSAT < 40%</td></tr>
<tr><td>E</td><td>Ferritin 200-800 ng/ml
and
TSAT 20-50%</td><td>Iron 100mg monthly unless contraindicated.
Check Fe studies 3 monthly</td></tr>
</table>

NURSE INITIATED IV IRON REPLACEMENT FLOW CHART (Dec 2010)


IRON DEFICIENCY
Ferritin < 200 ng/ml and TSAT < 20%
(Regime A)
Ferritin < 200 ng/ml and TSAT 20 - 50%
(Regime B)
Ferritin 200 – 800 ng/ml and TSAT < 20 %
(Regime C)
IV iron 100 mg each dialysis for 10 sessions (Maximum of 2 courses)
Repeat iron studies 1 month after each course
If, after 2 courses, Ferritin 200-800 ng/ml and TSAT still < 20% Revert to monthly dose and monitor iron monthly until review by Nephrologist
(Regime F)
If Hb > 120 g/L Ferritin 100 - 200 ng/ml and TSAT > 20% Revert to monthly dose and monitor iron monthly until review by Nephrologist
(Regime G)


IRON REPLETE
Ferritin
200 – 800 ng/ml
and
TSAT 20 – 50%
Maintenance course
IV 100 mg monthly unless contraindicated (Regime E)
Check iron studies 3 monthly
IRON OVERLOAD
Ferritin > 800 ng/ml
and/or
TSAT > 50 %
(Regime D)
Withhold IV iron for up to 3 months
Check iron studies monthly
Reinstate iron therapy when
Ferritin < 500 ng/ml or TSAT < 40 %
Hb > 120 g/L
Withhold ESA
Check Hb in 2 weeks
Restart ESA at a reduced dose or frequency when Hb < or = 120 g/L
Check Hb 2 weeks after any change in ESA dose
Aim for Hb
100 – 120 g/L
for all patients
Hb < 120 g/L
ESA dose may need review
Check Hb 2 weeks after any change in ESA dose

8. IRON SUPPLEMENTATION FOR PRE-DIALYSIS PATIENTS:

9. IRON SUPPLEMENTATION FOR PATIENTS ON PERITONEAL DIALYSIS:

See Flow Chart: Iron Replacement Protocol for Peritoneal Dialysis (Revised 2009)

IRON REPLETE:

[Ferritin 300 – 800 ug/L and TSAT 20 – 50%]

No IV Iron to be given

IRON DEFICIENCY:

[Ferritin < 300 ng/ml and/or TSAT < 20%]

- Maintain patients with a Ferritin > 300 ug/L in order to prevent iron deficiency occurring as booking appointments in ambulatory care can take time
- Iron levels may drop even further making iron and ESA management more complicated

Indications for intravenous iron infusion:

- Hb < 100 g/L
- Intolerance to oral iron
- Iron deficiency or suboptimal response to ESA therapy despite oral iron supplementation
- Last IV iron > 6 months ago
  - If < 6 months, consultant to review
- No blood loss

Intravenous iron infusion:

- Use a peripheral cannula
  - do not use arm containing AV fistula/ graft
- An AV fistula/graft must not be used for iron infusions

Recommended dosage schedule:

- 500 mg to 1000 mg of iron administered IV in a single infusion
- Alternatively, 250 mg IV iron weekly for 4 doses

Initial dose:

- Dilute dose in 500 mls 0.9% normal saline and infuse over 4 hours via an infusion control device at a rate of 15 mls/hr for the first 30 minutes
  - (set rate to 15 mls/hr and volume 7.5 mls)
- In the absence of a reaction, increase pump speed to 120 mls/hr

Subsequent doses:

- Dilute dose in 500 mls 0.9% normal saline and give over 4 hours
  - when unsure whether this is the patient's first dose or the first dose was given more than 12 months ago please use the initial dose regime.

Indications for not using IV Iron:

- Hb > 100 g/L
- Suspected or known allergies to Iron Polymaltose (Ferrosig) or Venofer

10. PATHWAY FOR ORGANISING IV IRON SUPPLEMENTATION FOR PRE-DIALYSIS AND PERITONEAL DIALYSIS PATIENTS

DOCTOR/NURSE:

1. Doctor to sign ACU (Ambulatory Care Unit) admission/referral form
2. State 1st dose or maintenance dose (any dose after the 1st dose)
3. Doctor to write internal script for iron
4. Nurse to call ACU and book appointment for patient – note the appointment time on the referral form
5. Fax referral form to ACU
6. Give original referral form and script to patient including a letter with instructions and contact details for ACU
7. All days available except Thursdays
8. Cost: Approximately $5 pensioner, $25 non-pensioner

PATIENT:

1. To contact ACU if they need to change or cancel their appointment
2. For 1st dose patients can expect a **full day admission** and will be in a **bed**
3. For maintenance dose (any dose after the 1st dose) patient can expect a shorter admission and will be in a **chair**

10.1 MONITORING IRON STATUS POST INFUSION:

Repeat Iron Studies and Hb 2 weeks post infusion or when bloods are next due

- **Ferritin < 300 ug/L or TSAT < 20%**
    - Investigate for blood loss or infection
    - Book second dose of iron
- **Ferritin 300 – 800 ug/L and TSAT 20 – 50%**
    - No further iron infusions
    - If Hb > 120 g/L decrease ESA
    - If Hb < 100 g/L increase ESA
- **Ferritin > 300 ug/L and TSAT < 20%**
    - No further action
    - Check Iron Studies when bloods next due

IRON OVERLOAD:

[Ferritin > 800 ug/L or TSAT > 50%]

- **Withhold iron for 3 months**
- **Recheck Iron Studies when bloods next due**
- **Investigate for other causes:**
    - Infection
    - Blood transfusions
    - Recent iron infusions

11. IRON SUPPLEMENTATION FOR HOME HAEMODIALYSIS PATIENTS:

[Ferritin < 200 ng/ml and TSAT < 20%]

During Home Training:

- As per ward protocol

When patient at home:

- Need for iron infusion is monitored by the Nephrologist
- Patient will self administer as per training or contact Syndey Dialysis Centre (SDC) for assistance
- Patient can attend Home Training for assistance if unsure of method

Indications for intravenous iron infusion:

- Intolerance to oral iron
- Iron deficiency or suboptimal response to ESA therapy despite oral iron supplementation

Intravenous iron infusion:

- Instructions for IV iron infusion given during home training or by SDC

Recommended dosage schedule:

- IV iron 100 mg each dialysis session for 10 consecutive sessions unless contraindicated
- Check Fe studies 1 month after completion of course or when bloods next due
- Once optimal iron parameters are achieved, titrate IV iron to monthly dose or as per Nephrologist

Initial infusion:

- Given during home training session or under supervision by SDC
- Dilute 100 mg IV iron in 100 mls 0.9% normal saline and infuse via an infusion control device at a rate of 15 mls/hr for the first 30 minutes (program pump for rate 15 mls/hr and volume 7.5 mls)
- In the absence of a reaction, increase pump speed to 120 mls/hr

Subsequent infusions:

- Call SDC or Home Training Nurse for assistance if unsure of method
- Draw up 100 mg IV iron into a 20 ml syringe and dilute to a volume of 20 mls with 0.9% normal saline
- Turn down blood flow rate to 200 ml per minute
- Swab arterial port and administer as a bolus slowly over 2 – 5 minutes towards the end of dialysis

12. PATIENTS ADMITTED FROM SUTHERLAND DIALYSIS UNIT:

On Admission to hospital:

- Check handover sheet from SDU for information on current ESA and Iron Regime: continue with same unless otherwise advised by the Renal team (document in RISC)
    - If the patient has already commenced a course of iron, continue the course unless otherwise indicated by the Renal team
    - If patient on monthly iron, continue same unless otherwise advised by Renal team
    - ESA and Iron doses will need to be charted on the inpatient medication chart

- On return to SDU, include the following on the handover sheet:
    - Date and dose of last iron given
    - Date and dose of last ESA given
    - If iron studies were attended and results

13. Evidence to support low dose maintenance IV Iron Supplementation:

- Most common factors associated with ESA hyporesponsiveness are iron deficiency, frequent hospitalization for infection, catheter use, hypoalbuminemia and elevated CRP levels (9)

- Assessment of IV iron to replete iron stores prior to ESA usage should be undertaken (5)

- IV iron therapy, when added to ESA therapy, offers additional clinical benefits, such as a reduction in the EPO dosing requirements needed to maintain improved Hb and hematocrit levels (4, 8, 9, 10)

- Losses of iron in haemodialysis patients can be up to 6 mg per day, exceeding the absorption capacity of the gastrointestinal tract (3)

- ESA use will increase the body's demand for iron and although sufficient iron stores exist, the iron cannot be delivered to the bone marrow fast enough to meet the increased iron demands (9)

- Inflammatory states increase the circulating level of 'hepcidin", an acute-phase hormone produced by the liver, which can block iron absorption from the gut and restrict the release of iron in storage – also known as inflammation-mediated reticulo-endothelial (RE) blockade (9)

- The administration of IV iron therapy (eg a 1 g repletion course) can mobilize iron, help overcome iron-restricted erythropoiesis/inflammation-mediated RE blockade and improve Hb levels (highlighted by improved levels of the iron marker reticulocyte Hb content [CHr]) – DRIVE Study (2007) (9)

- IV iron use in a patient with an active infection can facilitate microbial growth (9)

- DRIVE-II Study (2008) demonstrated a significant reduction in ESA dosing while maintaining a Hb level greater than 11 g/dL with the administration of IV iron (9)

- Regular, low dose IV iron can improve and stabilize Hb levels, preventing a "roller-coaster' effect which can result from a repletion course (9, 10)

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