ROYAL WOLVERHAMPTON HOSPITALS NHS TRUST

SHARED CARE PROTOCOL FOR ERYTHROPOIETIN USE
2016

New Cross Hospital	
Dr J Odum Consultant Physician & Nephrologist	**Dr S Cherukuri** Consultant Physician & Nephrologist
Dr P B Rylance Consultant Physician & Nephrologist	**Dr J Nicholas** Consultant Physician & Nephrologist
Dr P Carmichael Consultant Physician & Nephrologist	**Dr K Sandhu** Consultant Physician & Nephrologist
Dr S Acton Consultant Physician & Nephrologist	**Dr K Tan** Consultant Physician & Nephrologist
Dr B Ramakrishna Consultant Physician & Nephrologist	**Dr M Kamalnathan** Consultant Physician & Nephrologist
Walsall Manor Hospital	
Dr R Bavakunji Consultant Physician & Nephrologist	**Dr T Abdul Samad** Consultant Physician & Nephrologist

ERYTHROPOETIN - SHARED CARE PROTOCOL

INTRODUCTION TO ERYTHROPOETIN

Erythropoetin (recombinant human erythropoetin. Erythropoetin beta - Recormon, Boehringer Mannheim. Erythropoetin alpha - Eprex. Ortho - Biotech, Aranesp - Amgen) is licensed for the correction of erythropoetin deficiency in renal failure patients with anaemia. There is no clinical difference in the effect of the 3 forms of erythropoetin available.

ANAEMIA AND THE DIALYSIS PATIENT

Under normal circumstances the body compensates for reduced oxygen content in the blood due to, for example, blood loss or iron deficiency, by abruptly increasing renal erythropoetin production. However, in chronic renal failure such increases are not possible and chronic "renal anaemia" develops.

Endogenous erythropoetin (EPO), which is mostly produced in renal tissue, plays a central role in the production of erythrocytes. Low EPO production, related to reduced renal mass (as occurs in chronic renal disease), results in dialysis dependant patients with chronic renal failure developing a normocytic, normochronic anaemia. Also contributing to the anaemia may be blood loss, particularly in haemodialysis, shortened erythrocyte survival, iron deficiency, loss of folate and vitamin B12 through dialysis and sometimes aluminium intoxication.

The signs and symptoms of chronic renal failure (uraemia) are either caused or substantially aggravated by the anaemia. Symptoms of the anaemia include angina pectoris, heart failure, poor quality of life, lethargy, decreased exercise tolerance, lowered mood, interference with sleep/wake pattern and sexual function. These patients often have a low perception of wellbeing, life satisfaction and happiness.

THE TREATMENT OF RENAL ANAEMIA

Blood Transfusion

Repeated blood transfusions are successful at temporarily treating renal anaemia but are associated with three serious disadvantages:

1. Cytotoxic antibodies may be formed leading to complications during subsequent kidney transplantation.

2. There is a risk of transfusion related infections.

3. Regular transfusions can result in iron overload.

Erythropoietin Treatment

EPO therapy has been demonstrated in controlled trials to be highly effective and safe in raising patients' haemoglobin level and consequently correcting renal anaemia.

Objective and subjective benefits reported on patients in open trials are substantial and include improvements in energy, well-being, sleep/wake patterns, sexual function, perceived quality of life, decreased fatigue, shortness of breath and angina pectoris.

Quantitative assessments of patients on EPO therapy have revealed significant improvements in the degree of cognitive impairment, cardiac performance and energy levels. The need for regular blood transfusion is obviated in most transfusion dependant patients.

OTHER ASPECTS OF EPO THERAPY

Adverse Events

EPO therapy is safe with a low incidence of adverse events. Adverse events can be averted or ameliorated by regular monitoring of laboratory parameters and clinical observations. Patients are taught to recognise significant adverse events related to therapy and report these to the renal unit immediately.

Hypertension: believed to be due to an increase in blood viscosity and/or peripheral resistance is a recognised complication of correction and maintenance therapy. Patients with pre-existing hypertension should have this treatment and monitoring. Normotensive patients may develop hypertension but the increased incidence is of a low order as is that if worsening of pre-existing hypertension. In rare instances, in the early days of Erythropoietin treatment hypertensive crises with associated seizures have occurred. These episodes were usually preceded by severe headache, which should, therefore, be regarded as a possible warning symptom.

Thrombosis: of the Arterio-venous fistula may occur in connection with increased blood viscosity. Increased heparinisation may be needed during haemodialysis.

Flu-like symptoms: have been reported at the start of therapy.

Hyperkalaemia: increases in plasma potassium have been reported.

Functional iron deficiency: When EPO is commenced, a demand is placed on iron reserves by the increased erythropoiesis that results. Functional iron deficiency may develop in some patients and is avoided by giving iron therapy.

MONITORING ERYTHROPOETIN THERAPY

Monitoring of clinical and laboratory parameters is routinely performed in all patients, by the renal unit prior to commencing EPO, during initiation of EPO treatment and during the maintenance phase of treatment. Parameters which are monitored and the frequency of monitoring is as follows:

1. BP is measured routinely in all patients and E PO prescribed only when BP is <180/100. Blood pressure is measured at each haemodialysis (HD) session in patients undergoing regular HD (either 2 or 3 times weekly) during initiation and treatment phase.

For pre-dialysis and CAPD patients, blood pressure is measured by CAPD/Pre-dialysis nurses prior to initiation of treatment (as above) and measured weekly following initiation unit HAEMOGLOBIN rise has plateaued - usually 8-12 weeks after commencement of treatment. Thereafter pre-dialysis/CAPD patients with stable haemoglobin, blood pressure is measured monthly.

Any change in BLOOD PRESSURE is monitored and any necessary change in anti-hypertensive medication made. Should an increase in BLOOD PRESSURE continue to a value >200/110, EPO is discontinued until a satisfactory anti-hypertensive is achieved with medication. EPO will be re-introduced when blood pressure control is achieved.

2. FBC is measured monthly in all patients. The target haemoglobin aimed for with EPO treatment is 110-120 g/l.

A subtherapeutic response will require an increase in E PO dose and "supra" - therapeutic response will require a dose reduction.

Any dose change is made according to a strict protocol by a member of medical staff (either registrar or consultant) or by advanced nurse practitioners.

3. Plasma ferritin (as an assessment of iron deficiency) is measured in all patients prior to commencement of EPO. Inadequate plasma ferritin (<200ng/ml) is corrected with intravenous or oral iron supplementation prior to commencing EPO.

Similarly, functional or true iron deficiency may develop during treatment with E PO. Plasma ferritin is measured routinely in all patients on a 1-3 monthly basis and further iron supplementation (intravenous or oral) given when necessary).

4. Routine monitoring of electrolytes is performed by the renal unit.

5. Fistula patency is assessed routinely at each visit to the renal unit.

Routine regular monitoring will be undertaken by the renal unit. The general practitioner may be asked to assist in the monitoring process but this will always follow discussion with the specialist.

CRITERIA FOR PATIENT SELECTION FOR EPOETIN THERAPY

The majority of patients with renal failure are anaemic. At present the aim of the treatment is to treat patients in whom anaemia is a significant cause of symptoms. The following groups of patients should be treated - those:

i requiring regular blood transfusion

ii with angina or heart failure aggravated by anaemia

iii with haemoglobin concentrations < 100g/l

iv whose livelihoods are threatened by anaemia

v in whom transfusion is to be avoided to reduce sensitisation to transplantation antigens

vi in those with chronic kidney disease (GFR less than 60ml/min) or those on renal replacement therapy (haemodialysis, peritoneal dialysis or have organ transplantation).

DOSE AND ROUTE OF ERYTHROPOETIN ADMINISTRATION

To avoid waste EPO is prescribed in a whole vial /ampoule/ syringe doses given each

week to achieve an initial subcutaneous dose of approximately 150 units/kg/week. - For

Recormon or Eprex and 0.5 to 0.75 mg/kg per week for Aranesp. Subsequently the dose is adjusted

according to response to achieve a rate of rise in haemoglobin of not greater than

10g/l/month (correction phase). When the target haemoglobin level is reached the patient's symptomatic response is reviewed and the target levels re-adjusted if necessary. Once the individual patient's optimum haemoglobin level has been achieved it is maintained using EPO dose of approximately 30- 50% of the correction dose. This is subsequently titrated to the patient's response (maintenance phase).

THE REFERRAL DETAILS WILL STATE WHICH BRAND THE PATIENT HAS BEEN STABILISED ON (either EPREX or RECORMON or ARANESP).

SHARED CARE OF PATIENTS ON ERYTHROPOETIN THERAPY

Owing to the nature of the management of patients with end stage renal failure it is not possible to fully discharge the patients from the hospital back to their general practitioner. A system of shared care with shared commitments between hospital and GP has to prevail. The protocol outlines the referral procedure and areas or responsibility of the consultant or the registrar/ nurse practitioner on his behalf will contact the patient GP to invite participation in shared care and this should be done before the treatment is discussed with the patient.

Where the GP has agreed to undertake shared care, the patient will be given a letter with individual patients details and a copy of their EPO prescription to give to their general practitioner. This will indicate the dose and frequency and brand of EPO and brief clinical summary. The patient will be given TWO WEEKS SUPPLY of medication.

Through the process of monitoring the response to EPO, changes in haemoglobin and EPO dose will be sent to the general practitioners.

ASPECTS OF CARE FOR WHICH GP WILL BE RESPONSIBLE

Prescribing EPO beyond first two weeks treatment.

MONITORING OF PATIENT BY RENAL UNIT

Clinical monitoring, and chemical and haematology testing will be performed in all patients prior to, following initiation of treatment and during maintenance phase as described above.

AVAILABILITY OF CONSULTANT AND SENIOR MEDICAL/ NURSING STAFF FOR DISCUSSION

Renal Unit Telephone Number: 01902 695010 (direct line)

Chronic Kidney Disease Nurses: 01902 695466 (direct line)

Hospital Telephone Number: 01902 307999

The Nephrologist/ Registrar/ Renal Nurses can be contacted via the Switchboard