Short term Effect Of Intravenous Intermittent Iron Infusion versus Bolus Iron Infusion On Iron Parameters in Hemodialysis patients

Thesis

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Dedication

This work is dedicated to …

My beloved father, to whom I owe everything I ever did in my life and will achieve and making me the man, I am now

My mother for always being there for me

My brother and my sisters for their support

Finally I want to thank Dr. Eslam Shahein (My big brother for supporting).

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Mahmoud Salah

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INTRODUCTION

Intravenous iron is required in the majority of haemodialysis patients. There are two broad categories of intravenous iron therapy in haemodialysis patients

The current standard therapy is an intermittent divided doses of intravenous iron administration protocol **(Bailie et al., 2000)**.

A more recent trend is to consider a protocol of total dose correction of intravenous iron administration in one session of hemodialysis.

Such intermittent iron therapy can be administered via the dialysis machine heparin pump, as the doses and volumes are small and compatible with heparin infusion **(Yee and Besarah, 2002)**.

Intravenous iron therapy, was first described by **Granolleras et al. (1997)** who described an intermittent intravenous iron administration protocol for patients on regular haemodialysis,

There is no current evidence to demonstrate the benefits of a Proactive Protocol of intermittent Intravenous iron administration (PPCI), in an initiated protocol

delivered via the dialysis heparin pump, compared to bolus practice.

Chow et al. (2005) compared the efficacy and safety outcomes between a Protocol of total dose iron administration using iron sucrose (200 mg – 1000 mg) in one session of hemodialysis and a Protocol of Intermittent Intravenous iron administration by the co-infuse of 100 mg Iron per dialysis, in haemodialysis patients in a teaching Renal Unit with more than 300 dialysis patients.

They found that total dose correction successfully maintaine achieved Hb and iron parameters rapidly while allowing a small progressive reduction in EPO dose, compared to divide doses protocol, without the risk of iron overload.

The administration of Iron in large dose proved safe and no adverse reactions were detected (25 patients, > 1848 dialyses).

AIM OF THE WORK

This randomized controlled study has been initiated to investigate whether intermittent intravenous iron intake differs from a protocol of total dose correction iron administration, in terms of achieved Hb level or iron parameters and EPO requirement

RENAL FAILURE

Chronic kidney disease (CKD) is a progressive, irreversible process. The precise aetiology is often uncertain, but diabetes is the commonest cause of established renal failure (ESRF) in those starting dialysis. Hypertension, glomerulonephritis and pyelonephritis are less frequent causes. The presence of CKD is associated with an increased mortality risk **(Rachael and Iren, 2010)**.

Definition and classification:

CKD is defined as abnormalities of kidney structure or function, present for more than 3 months with implications for health. From 2004 the UK adopted the US Kidney Disease Outcomes Quality Initiative (KDIGO) definition and classification of CKD. Initially CKD was defined on the basis of an eGFR less than 60 ml/minute/1.73 m^2 or evidence of chronic kidney damage (irrespective of eGFR) for more than 3 months. In 2009 the albumin to creatinine ratio (ACR) was incorporated into the definition of CKD such that an ACR of 3 mg/mmol or higher on two occasions more than 3 months apart meant that CKD could be diagnosed in the presence of an eGFR greater than 60 ml/minute/1.73 $m^{2.}$ The 2013 KDIGO guideline defines CKD as the presence for more than 3

months of an eGFR less than 60 ml/minute/1.73 m^2 or one or more of the following markers of kidney damage:

- Albuminuria (albumin excretion ratio of ≥30 mg/24 hours; ACR ≥30 mg/g)
- Urine sediment abnormalities
- Electrolyte and other abnormalities due to tubular disorders
- Abnormalities detected by histology
- Structural abnormalities detected by imaging
- History of kidney transplantation.

CKD is classified on the basis of eGFR and ACR. ACR is classified into three groups and eGFR into six, by combining ACR and eGFR values patients can be assigned a risk of developing adverse outcomes related to CKD. This guides further treatment and management of their condition in an attempt to reduce the risk of progression, cardiovascular morbidity and mortality, and late presentation in end stage renal failure. ERF is defined as an eGFR of less than 15 ml/minute/1.73 m^2 (Kidney Disease: Improving Global Outcomes **(KDIGO) CKD Work Group, 2013)**.

Prevalence and progression:

The UK prevalence of stages III–V CKD is around 5%, with prevalence increasing with age mainly due to the accumulation of co-morbidities such as hypertension and heart failure. CKD benefits from early recognition, specialist management of the CKD and any associated co-morbidities. ERF is more prevalent in ethnic minority populations owing to the increased prevalence of type 2 diabetes and hypertension (Kidney Disease: Improving Global Outcomes **(KDIGO) CKD Work Group, 2013)**.

Complications of chronic kidney disease:

Cardiovascular disease:

Premature cardiovascular disease is the main cause of death in patients with CKD, accounting for almost half of all-cause mortality in ERF. The risk of cardiovascular events rises significantly below an eGFR of 60 and increases progressively with declining renal function. The actual diagnosis of AMI can be difficult as ECG abnormalities are common and cardiac troponins are raised even in the absence of ischaemia.

Cardiomyopathy is common in patients with CKD. Left ventricular (LV) hypertrophy results from hypertension and arteriosclerosis. Anaemia, fluid overload

and arteriovenous fistulae cause volume overload resulting in LV dilation. These changes in LV structure and the associated coronary artery disease lead to systolic and diastolic dysfunction. Mitral and aortic valve calcification occurs commonly as a result of metastatic calcium deposition, with secondary valvular dysfunction and conduction abnormalities. Infective endocarditis is more common in patients with CKD as a result of these valvular abnormalities and immunosuppression. Pericarditis associated with chronic pericardial effusions and tamponade can rarely occur in patients with end stage renal disease (Kidney Disease: Improving Global Outcomes **(KDIGO) CKD Work Group, 2013)**.

Hypertension:

Hypertension is extremely common in CKD, not only as a primer for the development of CKD, but also as a feature of disease progression with inadequate excretion of salt and water and increased renin production. Treatment to a level below 140/90 mm Hg is recommended to help reduce progression of CKD and the associated cardiovascular risk. Angiotensin-converting enzyme inhibitors and angiotensin receptor blocker drugs have an additional renal protective effect related to a reduction in proteinuria (Kidney Disease: Improving Global Outcomes **(KDIGO) CKD Work Group, 2013)**.

Haematological:

CKD-associated anaemia is normocytic and normochromic and associated with uraemia which reduces red blood cell life span. Erythropoietin-stimulating agents are generally used in those with a haemoglobin lower than 11 g/dl. Blood transfusion is avoided where possible due to the risk of fluid overload and of sensitization to donor lymphocytes which may make donor kidney compatibility more difficult in the future. Historically patients with CKD had an increased incidence of blood-borne viruses due to recurrent blood transfusions prior to screening of the donor population.

CKD is associated with an increased tendency to bleed, related to defective platelet adhesion and aggregation. Factors involved include an intrinsic platelet defect, abnormal von Willebrand factor (vWF) binding and increased parathyroid hormone levels. Platelet count and coagulation tests are generally normal, although bleeding time may be prolonged. Correction of anaemia, increasing vWF levels with desmopressin or cryoprecipitate, and haemodialysis (HD) are useful interventions to help reduce bleeding tendency (Kidney Disease: Improving Global Outcomes **(KDIGO) CKD Work Group, 2013)**.

Immune function:

Altered immune function is common in patients with renal failure. Suppression of T cell and humoral mediated immunity, an increase in pro-inflammatory cytokines, caused by uraemic immune dysfunction. Superficial infections are common, particularly in proximity to fistula sites and invasive lines. Post-operatively wound healing can be poor, with an increased frequency of wound infections (Kidney Disease: Improving Global Outcomes **(KDIGO) CKD Work Group, 2013)**.

Gastrointestinal tract:

Malnutrition and anorexia occur frequently in patients with CKD. Poor appetite is worsened by nausea and vomiting through uraemia and delayed gastric emptying due to autonomic dysfunction. Gastric mucosal irritation is common as is peptic ulcer disease along with an increased frequency of gastro-intestinal bleeding (Kidney Disease: Improving Global Outcomes **(KDIGO) CKD Work Group, 2013)**.

Neurological:

Patients with CKD are at an increased risk of both CNS and peripheral nervous system (PNS) abnormalities. CNS abnormalities may manifest as a change in behaviour,