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ORIGINAL RESEARCH ARTICLE

Prevalence of Renal Anaemia in Maintenance Hemodialysis Patients using Low Flux Versus High Flux Hemodialzer – A Comparative Study

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ABSTRACT

Background: Anaemia is a major complication in chronic kidney disease. Ideally anaemia should be lower in patients receiving High flux dialysis due to removal of middle to large molecular weight erythropoiesis inhibitors and few studies also support this. There has been no such study which compares the prevalence of anaemia in Low and High flux modalities with use of same High biocompatible membrane and same Ultrapure dialysis water for both. Both biocompatibility and Ultrapure water is known to have less systemic inflammation, hence better control of anaemia. This study aims to do so.

Materials and methods: For both Low and High flux modality High biocompatible Polysulfone or Polyamide membrane is used. Ultrapure dialysis water is used in both. Haemoglobin level have been measured monthly for consecutive three months and average reading have been compared in each group. Required dosages Iron and Erythropoietin also have been compared across the groups.

Results: In both Low Flux and High Flux modalities, significant percentage of the patients are having anaemia. While comparing, there is no statistically significant difference in prevalence of anaemia across the groups and Iron and Erythropoietin dosage also have no statistically significant difference.

Conclusion: In contrary to existing studies, it has been concluded here that if membrane biocompatibility is High for both the Low and High-flux modalities and same Ultrapure water is also used in both, there is no statistically significant difference in prevalence of anaemia in Low-flux and High-flux modalities of hemodialysis and required dosage of Iron and Erythropoietin also have no statistically significant difference.

Key words: Anaemia, Dialysis, Hemodialysis, Low-Flux, High-Flux

Introduction

Anaemia is one of the major complications of patients with chronic kidney disease (CKD) on or not on dialysis. Together with hypertension, fluid overload, it causes cardiac hypertrophy and subsequently cardiac dilation. As cardiovascular disease is the leading cause of morbidity and mortality in both dialysed and transplanted patients[1], as much as possible should be done to prevent and treat anaemia to reduce these cardiac complications.

Over recent years, the availability of recombinant human erythropoietin (EPO) therapy has led the almost complete disappearance of the severe anaemia of End Stage Kidney Disease (ESKD) patients requiring repeated blood transfusions[2]; it has also reduced left ventricular hypertrophy[3,4] and led to a direct improvement in heart function. These effects may delay the progression of heart disease and have already been associated with less overall and cardiovascular mortality and morbidity[5-7]. However, despite an increase in the use and

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average dose of EPO, a substantial percentage of patients do not achieve a haematocrit level of more than 30%[2,5–7].

CKD is a complex syndrome in which many factors other than absolute or relative Erythropoietin deficiency may contribute towards causing anaemia, such as the blood loss related to the dialytic procedure itself, and the haemolysis and bone-marrow suppression[8] probably induced by the retention of uremic toxins. Given the current availability of EPO, the other factors causing anaemia in CKD need to be considered.

Adequate dialysis is of utmost importance in correcting anaemia by removing small and possibly medium to large molecules, as the blood of CKD patients contains some substances whose molecular weight of 10000 Daltons, inhibits erythropoiesis. The biocompatibility of dialysis membranes is also probably involved[9].

Dialyzers are commonly classified as low- or high-flux membrane dialyzers. Low-flux membrane dialyzers are defined by an ultrafiltration rate <15 mL/mmHg/h and a β2MG clearance rate <15 mL/min[10]. High flux dialyzer is made of synthetic membranes with a higher permeability of middle molecules compared to low flux dialyzers. High-flux dialysis is defined as a β2- microglobulin clearance of over 20 ml/min.[11,12]

It is reasonable to postulate low-molecular-weight erythropoiesis inhibitors are removed by Low-flux membranes, (because anaemia improves after the start of dialysis even with low biocompatible cellulose membranes) and possibly medium to large-molecular weight inhibitors of 10000 Daltons are only removed by more permeable membranes. So, anaemia should be low in patients receiving High-flux dialysis and few studies[13,14] also confirms the same. But no study has clearly mentioned whether both Low and High flux were compared using same High biocompatible membrane or not. High biocompatible membrane is known to have reduced level of systemic inflammation, hence should have better control of anaemia.

Many hemodialysis centers where Hemodiafiltration is not done, uses standard RO water Dialysis Fluid (EDTA-ERA <100 CFU/ml and <0.25 EU/ml[15]), rather than Ultrapure water(EDTA-ERA <0.1 CFU/ml and <0.03 EU/ml[13]) for Low flux and High flux modalities in Hemodialysis. Ultrapure dialysis water is known to have reduced inflammation and better hemodynamic stability of patients.[16]

Therefore, this study has been planned to find out the prevalence of anaemia in maintenance hemodialysis (HD) patients using Low and High-flux dialyzers made up of same High biocompatible membrane (Polysulfone or Polyamide) and same Ultrapure dialysis water for both the Low and High flux modalities, and this study also compares the required doses of Erythropoietin and Iron across these two modalities.

AIMS AND OBJECTIVES

Aim:

To find out the prevalence of renal anaemia in maintenance hemodialysis patients using low flux versus high flux dialzer

Objectives:

1. To find out the prevalence of renal anaemia in maintenance hemodialysis patients using low flux versus high flux dialzer
2. To find out the dose requirement of Iron and Erythropoietin for renal anaemia in maintenance hemodialysis patients using low flux versus high flux dialzer

MATERIALS AND METHOD

Study design

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The study having prospective cross-sectional observational design has been done at the Department of Nephrology at Medica Super-specialty hospital, Kolkata, West Bengal, India.

Study duration

This study has been completed within 6 months, 3 months for patient selection and 3 months for follow-up.

Inclusion criteria

1. CKD patients of more than 18 years of age on maintenance hemodialysis.
2. For at least 3 months on hemodialysis since initiation.
3. On three sessions per week of HD with four hours each.

Exclusion criteria

1. Patients having AKI on dialysis.
2. Patients having other cause of anaemia like Gastro-intestinal bleeding.
3. Patients receiving less than 3 sessions per week of HD.

Operational definition

As per Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines, in dialysis and non-dialysis patients with CKD receiving ESA therapy, the selected hemoglobin target should generally be in the range of 11.0 to 12.0 g/dL.[17] So, a haemoglobin value of less than 11g/dL is taken as anaemia in this study.

Method of data collection

With those Inclusion and Exclusion criteria, 31 patients on Low flux and 31 patients on High flux were selected and followed up for three months. All cases have been evaluated with history and clinical examination. History regarding cause of CKD, whether kidney biopsy was done or not, drug compliance, compliance to fluid and salt restriction, have been taken.Haemoglobin level have been measured monthly for consecutive three months. Both prescribed dose of Iron and Erythropoietin have been administered by the staff of the dialysis unit, so that the compliance with the drug is ascertained. All the patients were on intra-venous multivitamin supplementation to restore the deficiency of dialyzable water-soluble vitamins.
All these patients have been evaluated for hemoglobin level and Erythropoietin and Iron requirements. Hemoglobin level has been monitored every month for consecutive three months and average have been taken and in both the groups findings have been compared.

RESULTS

Out of 62 patients 31 are in each group of Low and High flux modality. In Low-flux modality out of 31 patients 42% (n=13) are having normal hemoglobin level and 58% (n=18) are anemic(Figure1). In High-flux modality out of 31 patients 39% (n=12) are having normal hemoglobin level and 61% (n=19) are anemic (Figure1)

Comparison of Hemoglobin in Low-flux and High-flux modality

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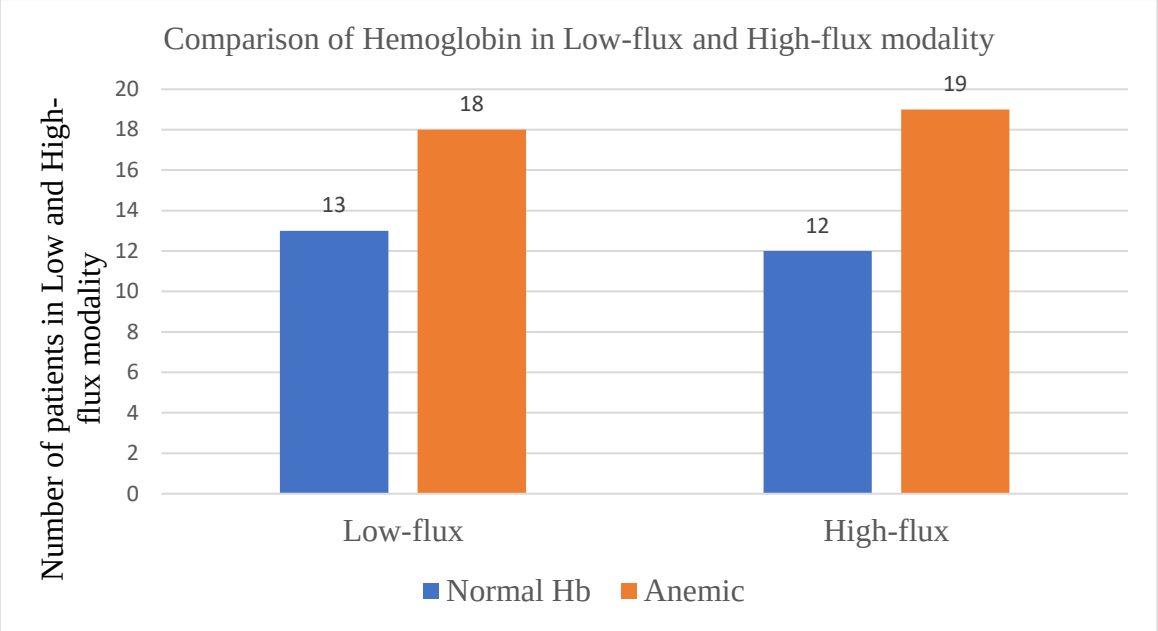

Fig: 1 – Columns showing comparison of Hemoglobin in Low-flux and High-flux modality

The study shows that in both Low Flux and High Flux modalities of dialysis, many of the patients are having anemia. While comparing, the p-value obtained is greater than 0.05(0.79). Hence, it has been concluded that there is no statistically significant association between Low-flux and High-flux modalities of hemodialysis and hemoglobin profile of patients.
The study shows that in respect to requirement of Erythropoietin dose, the p-value obtained is greater than 0.05 (0.26). Hence, it has been concluded that there does not exist any statistically significant difference in requirement of Erythropoietin across Low-flux and High-flux modalities of hemodialysis (Table 1)

Erythropoietin dosage across Low-flux and High-flux modality

	EPO requirement (IU/kg/week)	P-value
Low-Flux (n=31)	172.89±88.70	0.26
High-Flux (n=31)	197.84±87.60	

Table: 1 – Comparison of Erythropoietin dose in Low-flux and High-flux modality

The study also shows that in respect to requirement of Iron dose, the p-value obtained is greater than 0.05 (0.059). Hence, it has been concluded that there does not exist any statistically significant difference in requirement of Iron across Low-flux and High-flux modalities of hemodialysis (Table 2)

Iron dosage across Low-flux and High-flux modality

	Iron requirement (Mg/kg/week)	P-value
Low-Flux (n=31)	1.51±0.61	0.059
High-Flux (n=31)	1.41±0.52	

Table: 2 – Comparison of Iron dose in Low-flux and High-flux modality

DISCUSSION

In a prospective randomized study of **Ifudu*et al.*[13]** found that an increased dialytic dose in patients receiving inadequate dialysis led to a significant increase in their response to EPO; however, as this result was achieved using a highly permeable and biocompatible membrane

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(high- flux polysulphone), it is at least possible that biocompatibility or permeability, or both, have an additive effect to increased dialysis dose on the correction of anaemia. The results of **Villaverde *et al*.[14]** support this hypothesis. But none of the study had as comparable group with Low flux dialysis, which this study has. And here in this study the dialysis water used in both these modalities are of Ultrapure quality. Both High biocompatible membrane and Ultrapure dialysis water reduces systemic inflammation and hence better control of anaemia. It has been found from this study that with use of High biocompatible membrane and Ultrapure water, anaemia is not dependent on membrane flux.

Kobayashi *et al*.[18] have reported the clinical results obtained in eight haemodialysis patients treated with a large-pore membrane (BK-F polymethylmethacrylate) but, although they suggest a major effect in two patients with baseline haematocrit levels of approximately 21 and 22% (reaching only 25% at 11 months), these results cannot be considered conclusive for a number of reasons: the patients had a wide range of haematocrit levels and no information was given concerning their iron status; overall, the study was not randomized, the sample size was too small, there was no control group, and the eligibility criteria were unclear. The same considerations apply to the study of **Kawano *et al.*[19]**, and the study of **Villaverde *et al*.[14]**was not randomized. However, this study both prevalence of anaemia and dose requirement for Iron and Erythropoietin have been compared in both the Low and High flux group and it has been found that with use of High biocompatible membrane and Ultrapure water, anaemia is not dependent on membrane flux and Iron and Erythropoietin dose requirement also has no significant difference across Low and High flux group.

CONCLUSION

It has been concluded here that if membrane biocompatibility is High for both the Low and High-flux modalities and same Ultrapure water is also used in both, there is no statistically significant difference in prevalence of anaemia in Low-flux and High-flux modalities of hemodialysis and required dosage of Iron and Erythropoietin also have no statistically significant difference.

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