A CASE STUDY

Reduction of Erythropoietin Usage Associated with Installation of DSU Filters on Incoming Water Lines to Dialysis Machines Previously Equipped with Ultrafilters

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Background

Since the introduction of high flux dialyzer membranes, the quality of water for dialysis has become of greater concern. It is well known that cytokine inducing substances (CIS) in the dialysate can reverse filter across the high flux dialyzer membrane and into the patient's blood[1]. As a result, many patients tend to be in a chronically inflamed state with elevated levels of cytokines such as TNF-α and IL-6. These are known to inhibit response to erythropoietin stimulating agents (ESA) such as Epogen® (EPO).

Issue

In spite of the nearly 100% increase in EPO dosage over the last 10 years, patient Hgb levels have not increased. The average EPO dose in the US is >7000 units per treatment. More than 18% of the US dialysis patients receive dosages >35k units/week[2]. Until this year there has been a financial dis-incentive for treatment providers to address the issue of ESA response. Prior to the Medicare Improvements for Patients and Providers Act (MIPPA), the Centers for Medicare and Medcaid Services (CMS) reimbursed the use of injectable drugs at the Average Selling Price (ASP) + 6%. This essentially rendered the increased use of ESA's as a profit maker for the clinic. MIPPA sets reimbursement for the treatment costs, lab work and IV drugs into one bundled rate. While the implementation of the bundled reimbursement is being phased in over the next 3 years, providers must find a way to reduce ESA usage as soon as possible in order to continue to viably operate. Lowering the target hemoglobin has been considered. It has also been suggested to use ultrapure dialysate which has been shown in clincal trials to increase patient response to EPO by 17-34%[3,4]. However, a third and perhaps more easily imlementable option is presented in this study.

Objective

Observational study to determine if installation of the Nephros DSU filter on the incoming RO water line to the dialysis machine can result in improved patient response to ESA's beyond what is already being achieved with ultrapure dialysate such that lower doses of EPO are needed.

Methods

Two clinics took part in the study. Clinic A was equipped with Gambro Phoenix® machines using DiaClear™ ultrafilters. Clinic B was equipped with Fresenius 2008K machines using DiaSafe® ultrafilters. After a one month baseline period, Nephros DSU™ filters were installed on the RO water lines feeding these machines for a period of 6 months.

Forty eight (48) patients, 24 at each clinic took part in the study. Patients had stable hemoglobin levels, 11-12 and 10-12 g/dL for clinics A and B respectively, and stable EPO doses for at least 3 months prior to the study. Patients were treated with standard high flux bicarbonate dialysis.

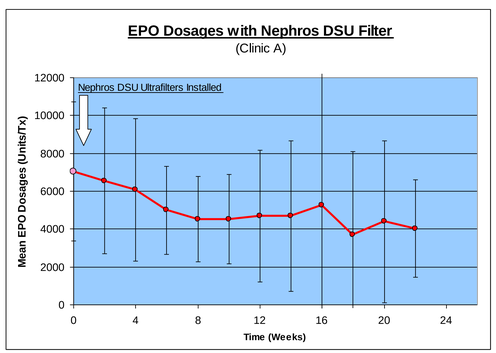
Hemoglobin and EPO doses were recorded at baseline and semi-monthly (Clinic A), or monthly (Clinic B). Appropriate changes to patient EPO doses were made according to the facility's standard protocol.

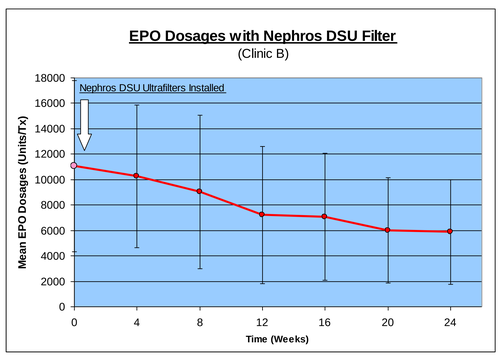
Twenty (20) patients completed the study at each clinic with dropouts due to transfer or non-compliance.

Results

For the 20 patients of clinic A, the average EPO dose decreased over 22 weeks from 7040 units per treatment to 4020 (43%, p = 0.008). Hemoglobin was stable (11.48 vs. 11.64).

For the 20 patients of clinic B the average EPO dose decreased over 24 weeks from 11052 units per treatment to 5900 (47%, p = 0.0002). Hemoglobin was stable (11.51 vs. 11.22).





Discussion

The addition of the Nephros DSU to the dialysis water treatment system was able to reduce EPO usage significantly in this prospective observational trial. Why such a dramatic decrease was observed despite the presence of conventional ultrafilters on the dialysis machine is unclear. The DSU filter uses a hydrophobic polysulfone membrane with a tighter pore structure than other ultrafilters. It is hypothesized that its additional redundant ultrafiltration stage facilitated the removal of smaller inflammatory substances that ordinarily pass through standard dialysate ultrafilters[5,6]. These substances could ignite low level inflammation and contribute to the inflammatory state and EPO resistance observed in hemodialysis patients. A more detailed study of patient inflammatory profiles using specific markers would help in determining the root cause of the observed EPO decrease.

However, regardless of the molecular mechanism, it does remain clear that the ESA responsiveness of these patients was dramatically improved. At the beginning of the study, Clinic A and B were spending $17k and $24k per month on EPO for their 20 patients respectively. At the end of the study, these monthly costs had decreased to $9.5k and $14k respectively. Pre-MIPPA the clinic would suffer financially for this improvement at the ASP+6% reimbursement. However, in the bundled rate system, Clinic A would see a $28 savings ($64 vs. $36) in average EPO cost per treatment. Clinic B would see a $40 savings ($94 vs. $54) on EPO compared to the baseline. These differences would have a significant positive financial impact on the ability of dialysis clinics to manage ESA costs thereby allowing clinics to thrive.

References

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