Can the Use of a Novel Dialysis Bloodline Increase Haemoglobin and Reduce Erythropoietin Doses?

Results of a Pilot, Crossover, Clinical Audit.

Iain C Macdougall,[1] Adam Rumjon,[1] Emmanuel Mangahis,[1] Leela Goldstein,[1] Thomas Ryzlewicz,[2] Franz-Ferdinand Becker,[2] William Kilgallon.[2]
[1]Renal Unit, King's College Hospital, London, United Kingdom; [2]Oxyless Ltd, Reading, United Kingdom.

Background

Current strategies for managing anaemia in dialysis patients include the use of erythropoiesis-stimulating agents (ESAs) and iron therapy which together increase the production of red cells in the bone marrow. An alternative approach, largely unexplored, is to try to prolong the survival of existing red cells.

It is well recognised that red cell survival is shortened in dialysis patients compared to normal healthy controls. Some individuals on dialysis have a red cell lifespan of around 70 days compared to the normal 120 days, and there are a number of reasons for this, including increased red cell fragility associated with the high levels of inflammation and oxidative stress present in the uraemic milieu.

The aim of the present investigation is to explore whether the use of a novel bloodline could improve the efficiency of ESA therapy in haemodialysis patients, possibly by improving red cell integrity and survival.

Bloodline Development

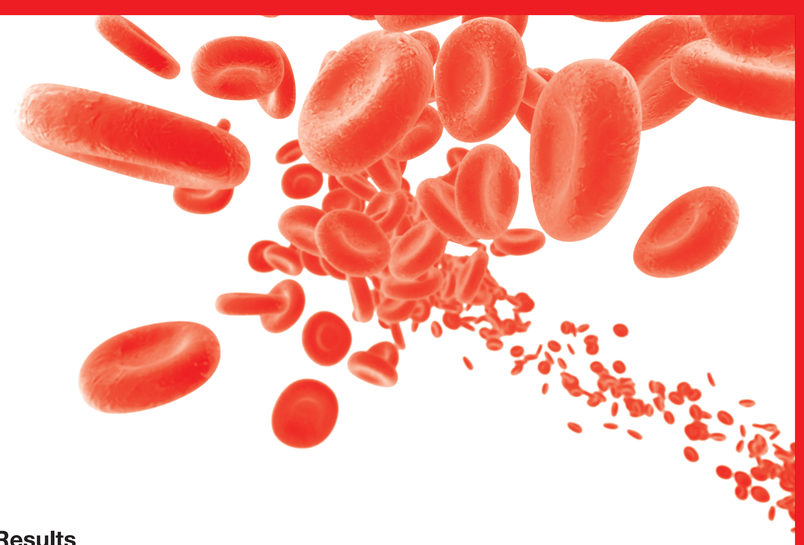
A novel universal bloodline (Oxyless) which reduces the contact between blood and air has been developed for routine haemodialysis (EU patent number EP 2022517, B1, and USA patent number US 8, 142, 384, B2) (Diagram 1). The overall reduction in blood-air contact in the arterial expansion chamber, compared to current bloodlines, is approximately 97%.

Hypothesis

The hypothesis is that a decrease in contact between blood and air will result in less shear stress on the red cell membrane. This might result in an increased red cell survival which, in turn, might lead to reduced ESA dose requirements.

Methodology

- 12-month open label, single crossover, cohort prospective audit
- Patients stable on HD for ≥ 3 months using B. Braun bloodlines
- >18 years of age
- Dialysis 3x weekly via an arterio-venous fistula
- All patients were treated with epoetin alfa and intravenous iron according to unit protocol
- Routine laboratory measurements were performed monthly
- Run-in baseline data was collected for 3 months prior to the audit
- Patients used the Oxyless bloodline for 6 months during the treatment phase and then reverted back to the control bloodline (B. Braun) for the crossover phase (6 months). Patients were followed for an additional 2 month extension at the end of the crossover phase.
- Haemoglobin, epoetin alfa dose, and ESA resistance index (ERI) were reported during the audit periods
- ERI was defined as the weekly ESA dose (IU) divided by the product of the patient's dry weight (kg) and the haemoglobin level (g/dL)



Results

Fifteen patients were initially entered into the audit as a pilot assessment. Data from only eight patients were able to be used as a result of drop-outs due to intercurrent events, including transplantation, gastrointestinal bleeding, acute inflammation, hospitalisation and resulting non-compliance.

Figure 1.
Hb levels and epoetin alfa doses during the Run-in, Treatment and Crossover phases

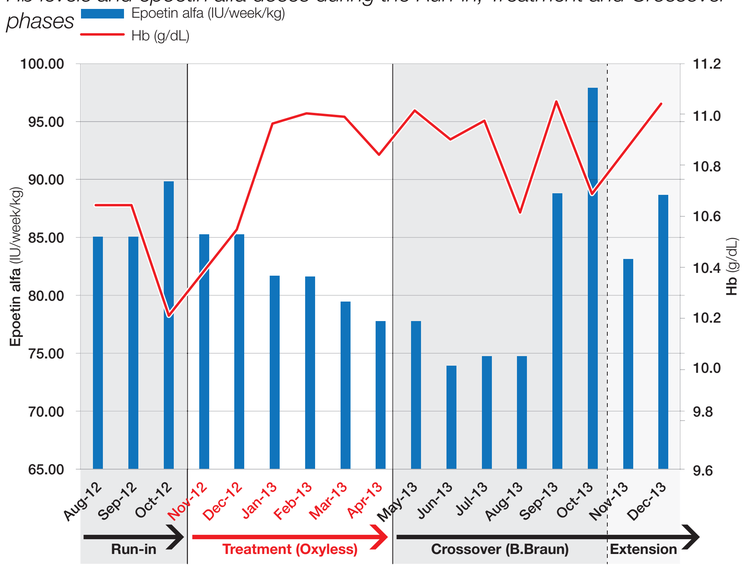


Figure 2.
Percent ERI change from Run-in (Aug-Oct 12) during the audit

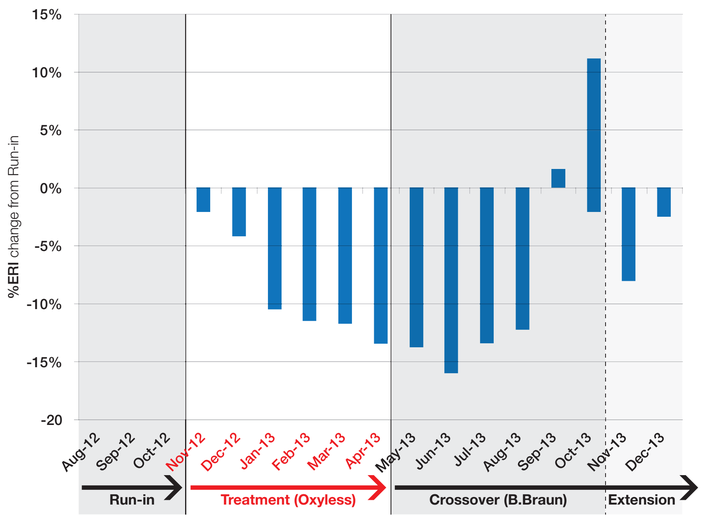
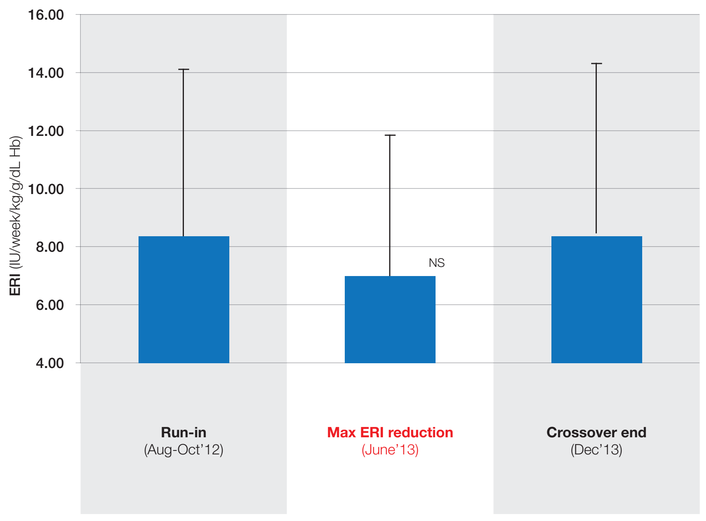


Figure 3.
ERI changes during the audit phases



Treatment phase with Oxyless bloodlines

- Haemoglobin (Hb) increased over a six-month period with three patients increasing by more than 1 g/dL *(Fig.1)*.
- The Hb increase was rapid in the first three months and stabilised at 11.0 g/dL for the latter half of the treatment phase.
- Epoetin alfa doses decreased steadily over the six month period from a mean of 86.5 to 77.8 IU/week/kg. This decrease continued during the first two months of the crossover to 74.0 IU/week/kg in June, month 8 *(Fig.1)*.
- Epoetin alfa dose reductions in five individual patients ranged from 14% to 67%, representing a total reduction of 12,667 IU/week and a per patient reduction of 2,533 IU/week.
- ESA resistance index (ERI) decreased steadily during the treatment phase *(Fig. 2)* with a maximum percent reduction of 16.2% achieved in month 8 (June).

Crossover phase

- In the first period of the crossover (May-July), mean Hb levels were maintained above 10.9 g/dL whilst mean epoetin alfa doses reduced to 74.8 IU/week/kg (375 IU/week) *(Fig.1)*.
- In August, Hb levels fell by a mean of 0.4 g/dL in total for all patients. These Hb reductions ranged from 0.1 to 1.3 g/dL with two patients' Hb reductions greater than 1 g/dL *(Fig.1)*.
- Between August and October, epoetin alfa doses increased from a mean of 74.8 to 98.0 IU/week/kg *(Fig.1)*, a mean increase of 23.1 IU/week/kg (1,750 IU/week).
- At the end of the crossover phase (October), epoetin alfa levels increased to a mean of 113% of run-in values in response to falling Hb levels *(Fig.1)*.
- During an extension of the crossover phase from November to December, epoetin alfa levels returned to 86.0 IU/week/kg (99% of run-in values) indicating a rebound effect. Mean Hb levels returned to 10.9 g/dL, which equates to 104% of run-in values.
- The ERI also increased during this phase *(Fig. 2)* and mirrored the rebound effect demonstrated in *Fig.1.*

ESA resistance index (ERI) changes

Figure 3 shows a reduction in ERI of 16.2% following the treatment phase with the Oxyless bloodlines compared to the run-in phase. This was observed in June and is consistent with a lag period of ESA response to Hb changes. Following the crossover phase, the ERI index returned to 97.5% of the run-in value.

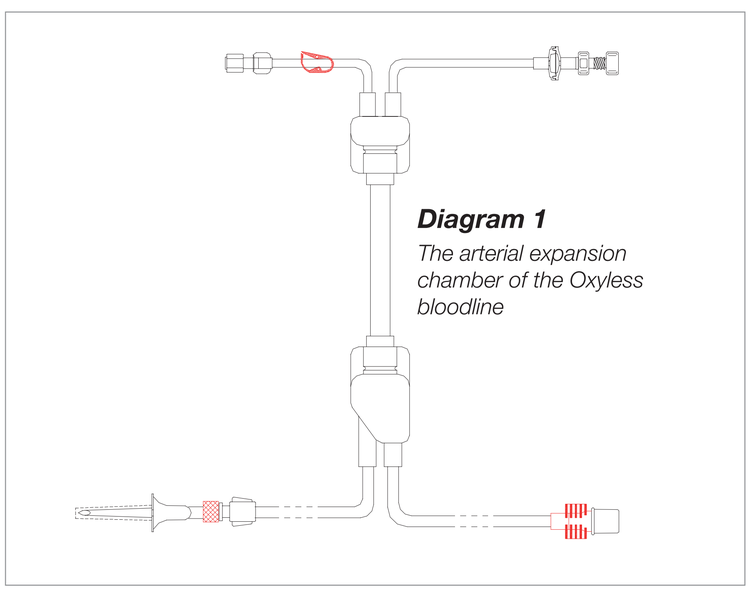


Diagram 1
The arterial expansion chamber of the Oxyless bloodline

Conclusion

The numbers completing this pilot assessment are too small to draw definitive conclusions. Nevertheless, there is a small but definite signal that the use of this novel bloodline may result in a reduction in ESA dose, and the crossover design allows some confidence in the validity of the data.

On the basis of these findings, a prospective multicentre European audit (PEMA) has now commenced in Portugal, Poland, Germany, Romania and the UK to gather more robust data on the impact of using the Oxyless bloodline on ESA dose requirements and costs.

Oxyless™

King's College Hospital NHS
NHS Foundation Trust