

# Online Haemodiafiltration

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## Goal

To review online haemodiafiltration (OL-HDF) and the advantages and disadvantages of this mode of renal replacement therapy.

### Objectives

- To define OL-HDF
- To review solute removal in OL-HDF
- Identify major clinical issues for OL-HDF treatments
- Identify benefits and risks associated with OL-HDF

## Background

Online haemodiafiltration is becoming a form of renal replacement therapy which is increasingly being used in the Australian context. It is thought to be a treatment which will provide better outcomes for those with ESRD. Many people on haemodialysis (HD) programs die within five years of commencing dialysis (Hodge 2010), and it has been suggested that a shift in the conservative dialysis paradigm should occur 'from the old goal of minimally adequate to a new goal of best possible' (Hodge 2010, pg. 5) for the treatment of ESRD. OL-HDF surely is a potentially 'best possible' treatment for all those with ESRD. Recent literature has reported that OL-HDF should be now considered as a viable renal replacement therapy which may have many beneficial effects for those with ESRD (Thomas & Jaber 2009).

The term haemodiafiltration was first used in 1977, following on from work which had been published in 1967 (Ronco & Cruz 2007). Now, through technological developments OL-HDF has

become an accepted therapy. OL-HDF has been described as the gold standard therapy as it combines both haemodialysis and haemofiltration, decreasing inflammatory responses and increasing middle molecule removal reducing 'the incidence of dialysis-related complications in long-term dialysis patients' (Canaud *et al* 2006, pg. S8).

## Solute Removal During Dialysis

During any dialysis procedure solutes are removed with a combination of diffusive and a low level, compared to OL-HDF, convective transport mechanisms. Haemodialysis relies, in the main, on diffusive processes and these rely upon solute concentration gradients on either side of the dialysing membrane, solute molecular size and the random speed of movement of solute molecules. This molecular movement 'is inversely proportional to molecular weight' (Canaud & Krieter 2007, pg. 265), i.e. the larger the molecule the slower the speed and the slower the clearance.

Haemofiltration relies upon convective transport and uses a current to sweep molecules of various sizes through the haemofilter membrane. 'The process of convection is more physiologic, as in the human kidney, plasma is filtered across the glomerulus, which is selectively permeable, and glomerular filtration relies on a relatively low hydrostatic pressure, convection, and solvent drag' (Thomas & Jaber 2009, pg. 611).

## Online Haemodiafiltration

OL-HDF is a renal replacement therapy in which the haemofilter consists of a very permeable membrane (i.e. high flux and high efficiency), and uses a combination of diffusion (haemodialysis)

and convection (haemofiltration) to increase the removal of solutes with a broad range of molecular weights. OL-HDF also requires a high blood flow rate through the extracorporeal circuit and a high dialysate flow rate. OL-HDF is categorised as a high efficiency therapy and as such a large volume of fluid is removed, and therefore requires replacement during the OL-HDF procedure. When compared to HD, OL-HDF uses a fivefold amount of replacement solution (Daugirdas *et al*. 2007).

The technological advances made, and now generally available, allow for those dialysis machines with OL-HDF capability to produce 'ultrapure' fluid which is reinfused during the OL-HDF session. 'Freshly prepared ultrapure dialysate is taken from the dialysate inlet line, processed with multiple filtration steps, and then reinfused [into the extracorporeal circuit] as replacement fluid' (Ronco & Cruz 2007 pg. 236) and therefore allows for high fluid turnover and better solute removal.

Water quality is vital to prevent hazardous endotoxins or bacteria entering the extracorporeal circuit and therefore the patient (Colussi & Frattini 2007). Water which is delivered to the OL-HDF machine has been shown to be safe with studies reviewed by Canaud *et al* (2006) reporting no incidence of pyrogenic reactions from the administration of large amounts of infusion fluids. Ultrapure replacement fluids can be generated 'for a prolonged period of time, provided that quality standards for water treatment systems and microbiological monitoring are satisfied' (Penne *et al* 2009 pg. 670). Of more than 11,000 OL-HDF treatments there were no reported side

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effects (Penne *et al* 2009). The fluid replacement can be either before the haemofilter (pre-dilution) or after the haemofilter (post-dilution), each of these have clinical issues to be considered.

The decision to commence OL-HDF therapy for patients is generally based on the need for a more efficient dialysis versus the increased cost of OL-HDF. It is estimated that OL-HDF costs \$US20.00 more per treatment than conventional haemodialysis (Petrie *et al* 2008). However, this relatively small cost should be weighed against costs of treatment and hospitalisation for medical conditions such as increased cardiovascular morbidity and mortality and acquired amyloidosis both of which can be ameliorated with the use of OL-HDF. Currently, generally speaking, it is those who have a large body surface area, have been on dialysis for a long time and therefore at a higher risk of amyloidosis and its consequences, or who have severe cardiovascular instability with conventional dialysis therapy (Munoz *et al* 2006) who are more likely to be commenced on OL-HDF.

**Clinical Issues for Online Haemodiafiltration**

Canaud & Krieter (2007 pp. 266-269) point out various considerations, benefits and risks for OL-HDF therapy these include:

1. The maintenance of ‘ultrapure’ replacement fluid during OL-HDF by monitoring water quality on a regular basis (at least monthly) and comparing results to best practice guidelines for dialysis water quality.
2. Evaluation of pre-dilution versus post-dilution method for replacement fluid. ‘Predilution limitations include dilution of blood side solute concentration and reduced small solute clearance; post-dilution limitations are haemoconcentration increased fibre clotting, and protein denaturation’ (Thomas & Jaber 2009, pg. 612).

There is now real concerns around the increased viscosity of blood

which occurs in OL-HDF and its association with cardiovascular morbidity and mortality, especially in those with a high risk. ‘Endothelium shear stress interaction associated with blood viscosity promotes secretion of vasoactive mediators and vascular remodeling factors and both mechanisms are associated with the accelerated atherosclerotic process seen in many CKD patients’ (Canaud *et al* 2010 pg. 437).

3. Ultrafiltration and sodium profiling; and blood volume monitoring can still be done in OL-HDF.

**Therapy.**

4. Assessment of vascular access capability as a blood flow rate of at least 350 mls./minute is required for OL-HDF.
5. The use of a biocompatible high flux high efficiency dialysing membrane.
6. High blood flows and dialysate and/or infusate flows which will increase solute removal.
7. Anticoagulation may need modification because of the increase in blood viscosity.

**Reported Benefits of OL-HDF**

- Decreased mortality and morbidity
- Better haemodynamic stability

- Better blood pressure control
- Increased biocompatibility due to ‘the combined use of synthetic biocompatible membrane, ultrapure dialysis fluid, and “passivation” of the membrane by the protein coating layer’ (Canaud *et al* 2006, pg. S8).
- Decrease in systemic inflammatory markers
- Better removal of middle molecules (e.g.  $\beta$ microglobulin, phosphate)
- Delays onset of  $\beta_2$ -M-amyloidosis because of better  $\beta$ microglobulin removal
- Improved dialysis efficiency for both small and middle molecules
- Improved lipid profile
- Improvement in anaemia possibly as a result of the removal of erythropoietic inhibitor substance and reduced inflammatory response
- Improvement in nutritional status

**Risks of OL-HDF**

- Water/dialysate/infusate fluid contamination
- Protein loss
- Essential vitamin loss
- An increased risk of cardiovascular morbidity and mortality due to an increase in blood viscosity.

**Key Messages for OL-HDF**

- Water quality delivered to the OL-HDF machine must meet best practice guidelines
- Routine sampling of reinfusion fluid for contaminants
- There are risks associated with haemoconcentration during OL-HDF with the post-dilution method for replacement fluid
- Vascular access should deliver  $\geq$  350 mls/minute
- Anticoagulation may need modification to reduce risks associated with haemoconcentration.
- Monitor nutritional status of those patients on OL-HDF because of potential protein and essential vitamin loss.

### Learning Activities

1. Locate your HD unit's latest water analysis results and compare these with the current AAMI standards (a copy of this should be available in your unit – or from the biomedical technicians). How do the water results from your unit compare?
2. How often does your unit test the OL-HDF reinfusion fluid to assess for any contaminants?
3. How many patients are on OL-HDF in your unit, and what was the rationale for commencing these people on OL-HDF? Were the reasons for commencing OL-HDF because of the need for better dialysis efficiency, large body size, or cardiovascular instability with conventional HD therapy?

### Conclusion

OL-HDF is reported to have many positive outcomes for those with ESRD and who are on haemodialysis programs. However, there is still some controversy in regard to the patient outcomes, and although there is more research being done, more conclusive research is needed. In conclusion there needs to be more quality studies undertaken to compare patient outcomes in HD and HDF modalities 'and these studies should focus on cardiovascular morbidity and mortality as primary endpoints' and more emphasis be on the clearance of 'middle' molecular size substances 'with validation of middle molecule clearance markers' (Thomas & Jaber 2009, pg. 614).

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### Review Questions

1. Solute removal in OL-HDF occurs by which one (1) of the following?
  - a. haemodialysis and haemofiltration
  - b. haemodialysis and hydrostatic pressure
  - c. haemofiltration and haemoconcentration
  - d. haemodialysis and haemoconcentration
2. Increased biocompatibility has been reported with the use of OL-HDF. This is due to the use of which one (1) of the following?
  - a. Ultrapure fluid
  - b. 'passivation' of the dialysing membrane
  - c. a synthetic biocompatible dialysing membrane
  - d. all of the above
3. It has been reported that the onset of  $\beta_2$ -M-amyloidosis may be delayed with the use of OL-HDF. This is most likely due to which one (1) of the following? OL-HDF:
  - a. increases the removal of small solutes
  - b. decreases the removal of small solutes
  - c. decreases the removal of middle molecules
  - d. increases the removal of middle sized molecules
4. It has been reported that OL-HDF improves a patient's anaemic status. The improvement in anaemia may be due to all of the following EXCEPT:
  - a. improved urea and creatinine clearances
  - b. an increase in dose of EPO required in OL-HF
  - c. a reduction in systemic inflammatory response
  - d. the removal of an erythropoietic inhibitor substance
5. The replacement fluid required in OL-HDF can be given either by the pre-dilution or post-dilution method.

- A limitation of the pre-dilution method is which one (1) of the following?
- hamoconcentration
  - haemofilter fibre clotting
  - decreased small solute removal
  - higher risk of contamination of the extracorporeal circuit.
6. The replacement fluid required in OL-HDF can be given either by the pre-dilution or post-dilution method. A limitation of the post-dilution method is which one (1) of the following?
- increased blood viscosity
  - decreased small solute removal
  - decreased middle molecule clearance
  - higher risk of contamination of the extracorporeal circuit.
7. It is important that the nutritional status of patients who are having OL-HDF is monitored. The rationale for this is which one (1) of the following?
- chronic effects of reinfusion fluids
  - effects of increased anticoagulation needs
  - the ability of OL-HDF to denature proteins
  - loss of protein and essential vitamins during OL-HDF sessions
8. There is a potential risk for contamination of the reinfusion fluid required in OL-HDF. This risk is reduced markedly by which one (1) of the following?
- reinfuse fluid via the post-dilution method
  - adding broad spectrum antibiotics to the reinfusion fluid
  - replacing the reverse osmosis membrane on a monthly basis
  - ensuring the water delivered to the OL- HDF machine meets the best practice guideline for dialysis water quality
9. If the reinfusion fluid was contaminated, a patient would generally exhibit a clinical picture consistent with which one (1) of the following?
- a pyrogenic reaction
  - a pulmonary embolism
  - an acute cardiac event
  - a hypotensive episode
10. Which one (1) of the following is not a key consideration for OL-HDF?
- assessment of anticoagulation needs
  - increased need for sodium replacement
  - routine sampling of reinfusion fluid for contaminants
  - a vascular access which delivers a BFR of > 350 mls./min.

### Answers to Review Questions

Question	Answer
1	a
2	d
3	d
4	b
5	c
6	a
7	d
8	d
9	a
10	b



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