The Effect of Convection on the Clinical Status of Hemodialysis Patients

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Dialysis treatments have allowed "terminal patients" to live for years and years. However, life expectancy and quality are still consistently reduced in renal dialysis patients. Consequently, all efforts to provide alternative treatments to the conventional ones are highly justified. Recently, the Hemo Study showed that neither the use of high-flux membranes, nor the increase of the dialysis dose above the conventional, were able to reduce significantly mortality and morbidity of patients, although 8% reduction of the risk of death was seen in patients treated with high-, when compared with patients treated with low-flux dialysis. Thus, a relevant question is if convective treatments may offer an "overprotection" from morbidity and mortality, in comparison with low- and high-flux treatments. Except for a better cardiovascular stability observed in hemofiltration and a higher β_2-microglobulin clearance given by on-line hemofiltration and hemodiafiltration, evident clinical benefits of convective treatments, when compared with the conventional high-flux treatments, are not yet clearly demonstrated. That notwithstanding, on-line convective treatments, that are performed with high-flux compatible membranes and high-technology machines, producing high-quality water, offer at the moment the best basis for the improvement of clinical results of dialysis, especially in some categories of patients.

Convective Treatments

- High - flux hemodialysis
- Hemodiafiltration - online hemodiafiltration
- Hemofiltration - online hemofiltration

Main Characteristics of Convective Treatments

- ***MEMBRANES***
- TRANSPORT CHARACTERISTICS
- ULTRAPURE DIALYSATE AND SUBSTITUTION FLUID

Main Characteristics of Convective Treatments

- ***MEMBRANES***

High - flux semisynthetic and synthetic

Characteristics:
- high permeability
- high biocompatibility

Main Characteristics of Convective Treatments

- MEMBRANES
- ***TRANSPORT CHARACTERISTICS***
- ULTRAPURE DIALYSATE AND SUBSTITUTION FLUID

Main Characteristics of Convective Treatments

- ***TRANSPORT CHARACTERISTICS***

Convective removal of water and electrolytes and higher clearance of middle and larger molecular weight solutes

Main Characteristics of Convective Treatments

- MEMBRANES
- TRANSPORT CHARACTERISTICS
- ***ULTRAPURE DIALYSATE AND ULTRAPURE SUBSTITUTION FLUID***

Main Characteristics of Convective Treatments

- ***ULTRAPURE DIALYSATE AND ULTRAPURE SUBSTITUTION FLUID***

The use of ultrapure dialysate and of new online systems for production of microbiologically safe substitution solutions may have a favourable effect on patient outcome

Main Characteristics of Convective Treatments

Since convective treatments are usually performed with synthetic biocompatible membranes, it is hard to separate the effect of convection from the effect of biocompatibility

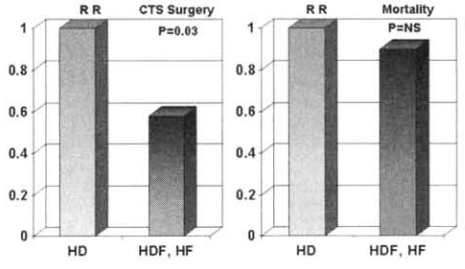
Clinical Advantages of Convective Treatments

It is a widespread opinion that convective treatments give a clinical advantage over standard diffusive hemodialysis, when considering the physiological outcomes

Superiority of Convective Treatments?

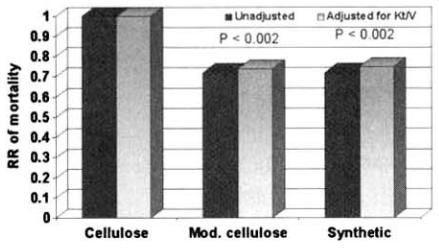
The crucial point is to demonstrate the superiority of these dialysis techniques on major outcomes: morbidity, mortality and quality of life

Effect of convective treatments on outcome



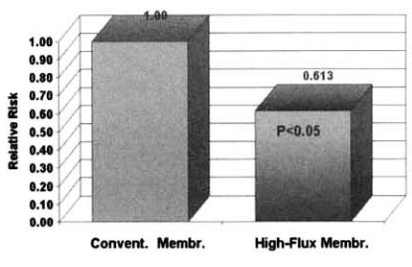
Locatelli F et al, Kidney Int 55: 286, 1999

Effect of Dialysis Membrane on Mortality



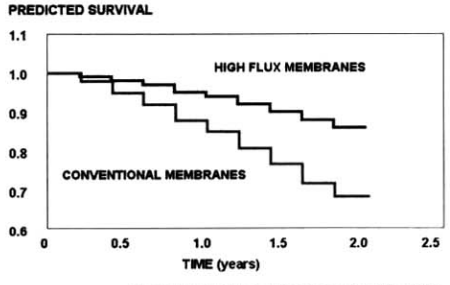
Hakim RM et al, Kidney Int 50: 566, 1996

Effect of Dialysis Membrane on Mortality



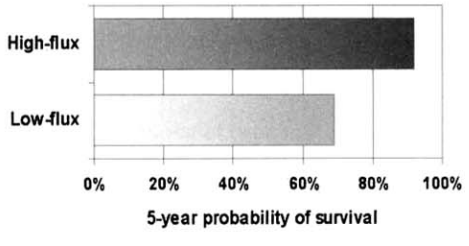
Koda Y et al. Kidney Int 52: 1096, 1997

Dialysis Membranes and Survival



Hornberger et al. J Am Soc Nephrol 3: 1227, 1992

Effect of Membrane Permeability on 5-Year Survival



Woods et al. Nephrology, 1997

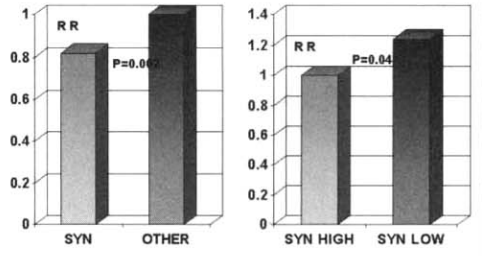
Dialysis Membranes and Causes of Death

Adjusted Relative Mortality Risk: Proportional Hazards Model

CAUSE OF DEATH	DEATH (No.)	R R (SYN/CEL)	P value
CORONARY ART. DIS.	182	0.74	0.07
OTHER CARDIAC	407	0.86	NS
CEREBROVASCULAR DIS.	60	1.08	NS
INFECTION	168	0.69	<0.03
MALIGNANCY	38	0.90	NS
OTHER	300	0.82	<0.05
MISSING	100	0.90	NS
ALL CAUSES	1255	0.82	<0.002

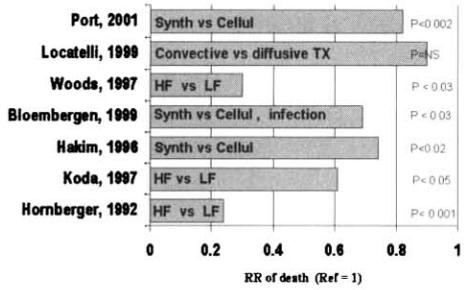
Bloembergen WE et al, Am J Kidney Dis 33: 1, 1999

Effect of convection and membranes on mortality



Port FK et al, AJKD 37: 276, 2001

CONVECTION & MEMBRANES AND MORTALITY



Middle molecules and mortality

Using vitamin B12 as a surrogate for middle molecules, analysis of data from the 1991 case mix adequacy study of the USRDS found that the group with a 10% higher calculated vitamin B12 removal had a 5% lower death risk ($p < 0.0001$).

Leypoldt JK et al, AJKD 33: 349, 1999

The US H E M O Study

Randomized clinical trial in 1846 patients undergoing thrice - weekly dialysis, using a two-by-two factorial design to assign patients randomly to a standard or high dose of dialysis and to a low-flux or high-flux dialyzer

Eknoyan et al, NEJM 347: 2010, 2002

The US H E M O Study

randomized multicenter trial 2 x 2 factorial design

HD DOSE	Standard	High
* eKt/V	1.16	1.53
spKt/V	1.32	1.71

MEMBRANE	Low flux	High flux

*eKt/V from the formula of Daugirdas-Schneditz validated in the pilot phase of the study

G Eknoyan et al, NEJM 347: 2010, 2002

The US H E M O Study

- The primary outcome, death from any cause was not significantly influenced by the dose or flux assignment
- The main secondary outcomes also did not differ significantly between either the dose groups or the flux groups

Eknoyan et al, NEJM 347: 2010, 2002

The US H E M O Study

CONCLUSIONS

1. Increasing Kt/V_{urea} in a thrice-weekly schedule
2. Changing to high-flux membranes

do not improve mortality or reduce hospitalizations

Eknoyan et al, NEJM 347: 2010, 2002

CONCLUSIONS

Even though almost all available studies support the hypothesis that convection & high-flux, biocompatible membranes are associated with reduced morbidity and mortality risks

to date there is no absolute proof showing a cause - effect relationship between convection & high-flux, biocompatible membranes and the outcome of dialysis patients.

CONCLUSIONS

This lack of evidence is due to the absence of long - term randomized clinical trials.