

Hemofiltration and Hemodiafiltration Reduce Intradialytic Hypotension in ESRD

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JASN 2010

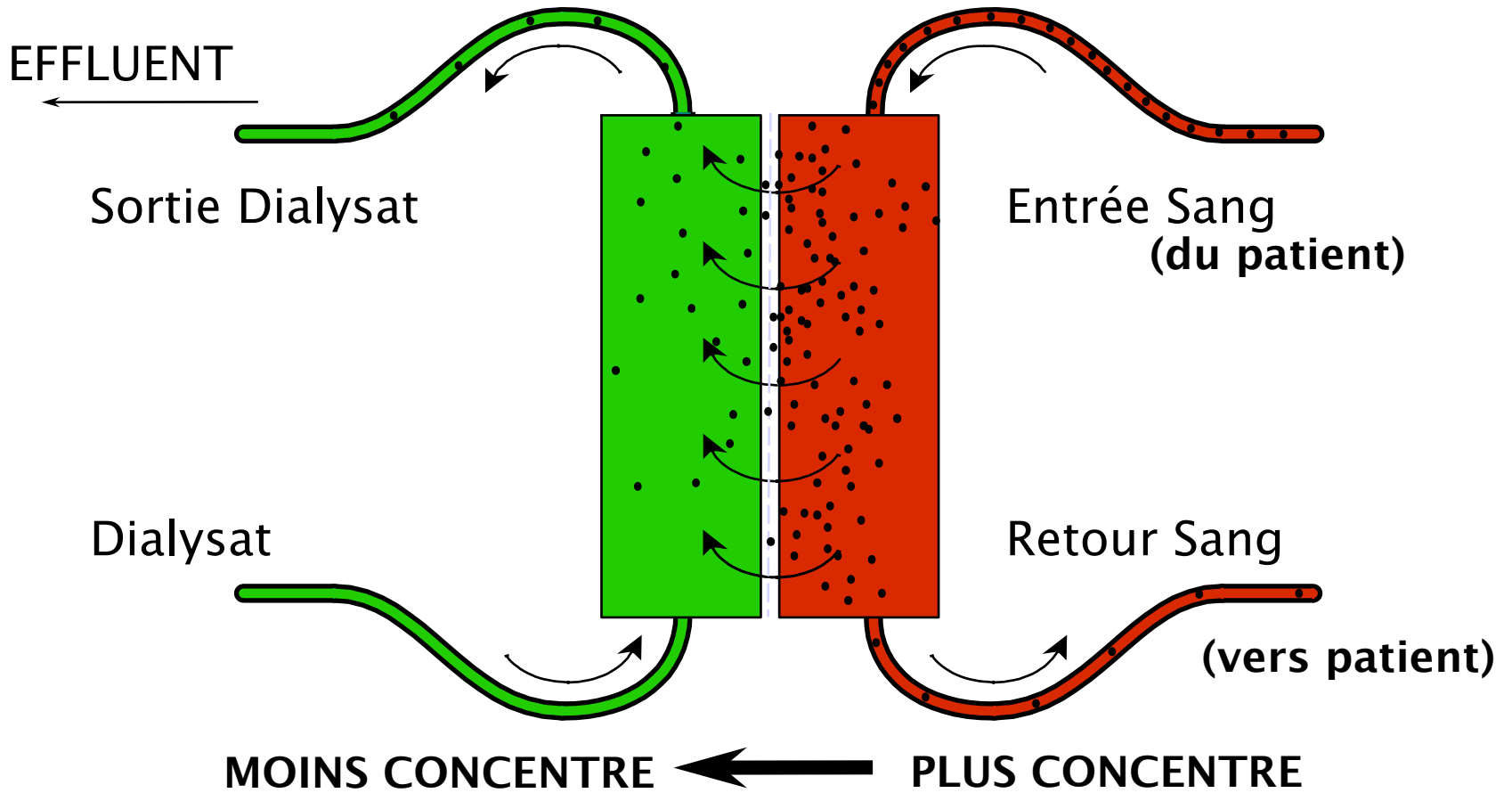
Journal club du 04.11.2010 P.Saudan

Rationnel

- Hypotension intradialytique symptomatique très fréquente en HD
- RCTs (HEMO *NEJM* 2002 MPO *JASN* 2009) Avantage de survie chez des sous-groupes de patients
- Meilleure survie avec traitement convectifs (DOPPS *KI* 2008)
- Etudes Sardinian Collaborative group: moins ISH avec ttt convectifs
- **Essai Prospectif randomisé comparant plusieurs méthodes de dialyse avec ISH comme critère de jugement clinique**

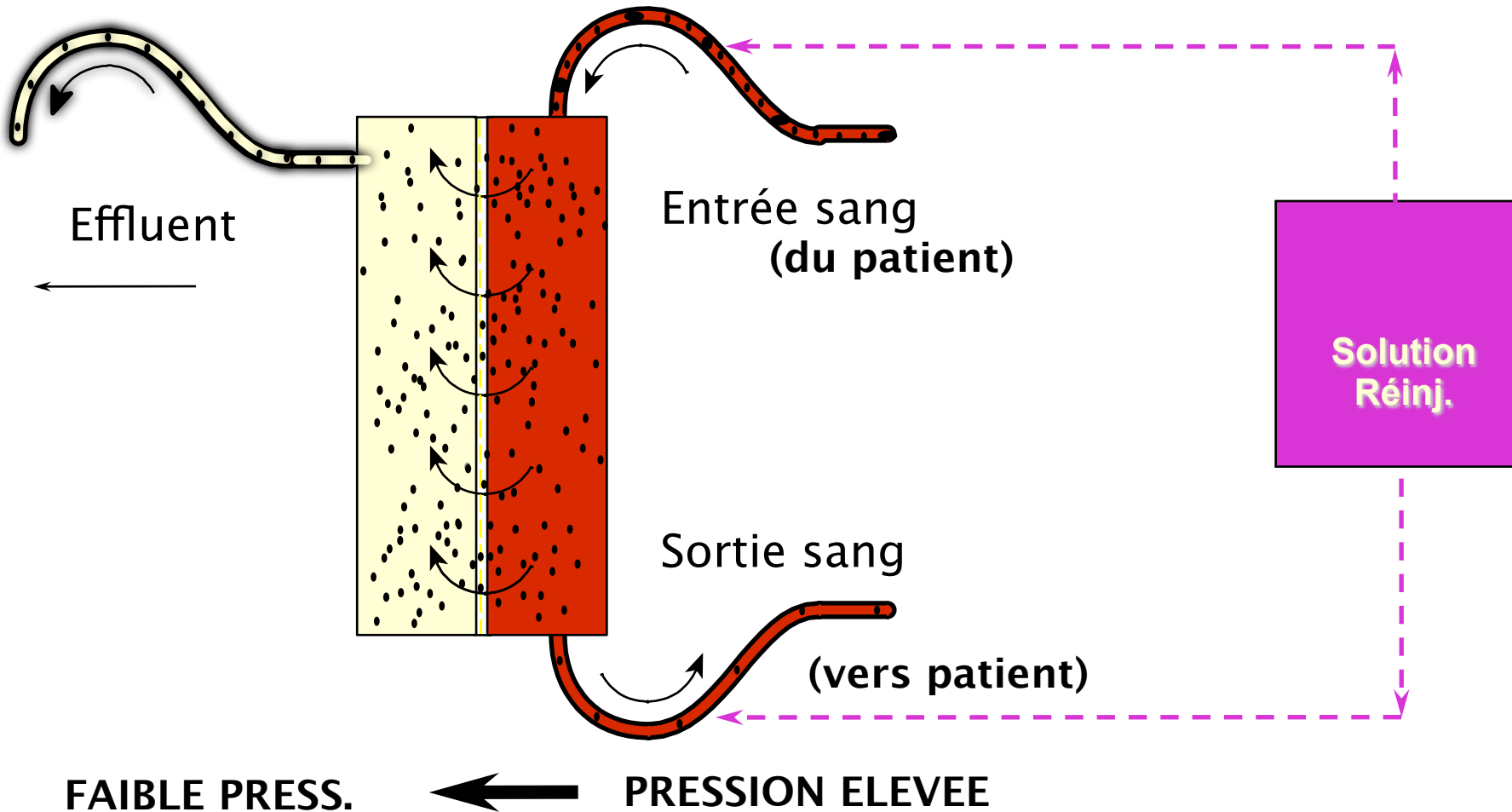


HEMODIALYSE



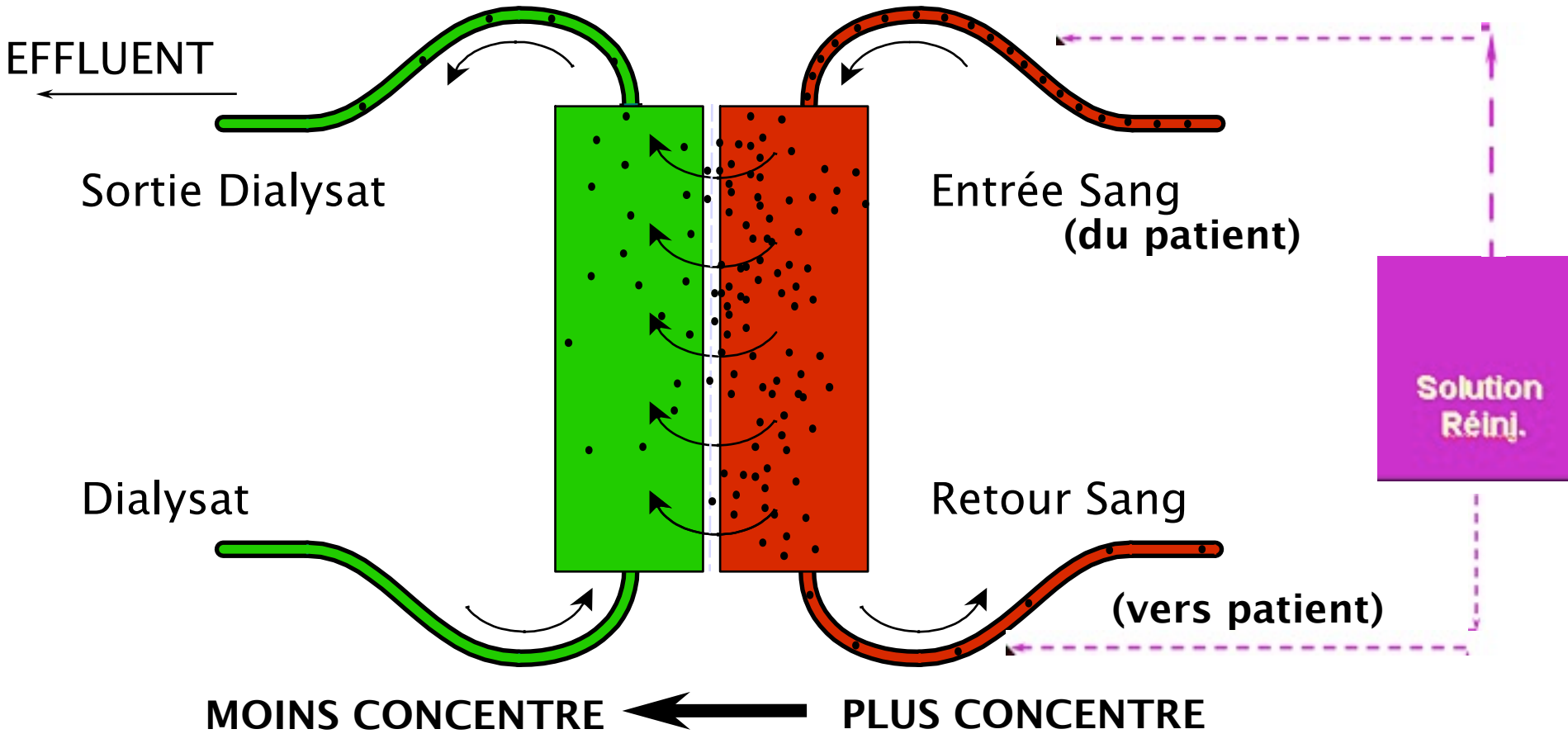


HEMOPILTRATION





HEMODIAFILTRATION



Hypothèse de recherche

- Diminution de la fréquence d'ISH avec les techniques convectives (hémofiltration ou hémodiafiltration) versus HD standard

Dessein de l'étude

- Multicentrique, open-label, randomisé
- Période de recrutement augmentée d'une année à 4 ans
- Critères inclusion: 18-80 ans, HD ou HDF depuis 6 mois, PC < 90kg, clin stable. Exclusion: diurèse > 200 ml/24h, affections actives, dysfonction accès vasc avec débit sg < 300 ml/mn
- 2 mois run-in (standardisation T°, teneur NA et

Caractéristiques des patients (1)

Table 1. Clinical characteristics of enrolled patients at baseline

| Characteristic | Total (N = 146) | HD (n = 70) | Pre-HF (n = 36) | Pre-HDF (n = 40) | P |
|---|---------------------|---------------------|---------------------|---------------------|-------|
| Gender (n [%]) | | | | | 0.646 |
| male | 84 (57.5) | 43 (61.4) | 19 (52.8) | 22 (55.0) | |
| female | 62 (42.5) | 27 (38.6) | 17 (47.2) | 18 (45.0) | |
| Age (years; median [IQR]) | 67.4 (58.1 to 73.3) | 65.2 (58.1 to 70.8) | 71.3 (60.6 to 74.4) | 66.8 (54.6 to 74.3) | 0.086 |
| Body weight (kg; median [IQR]) | 64.9 (55.9 to 70.8) | 65.5 (57.9 to 70.8) | 62.3 (53.3 to 66.6) | 66.8 (55.4 to 76.9) | 0.115 |
| Hypertension (n [%]) | 83 (56.8) | 39 (55.7) | 20 (55.6) | 24 (60) | 0.894 |
| Diabetes (n [%]) | 26 (17.8) | 12 (17.1) | 3 (8.3) | 11 (27.5) | 0.091 |
| Insulin therapy (n [%]) | 16 (11.0) | 8 (11.4) | 0 (0.0) | 8 (20.0) | 0.020 |
| Ischemic cardiopathy (n [%]) | 32 (21.9) | 16 (22.9) | 6 (16.7) | 10 (25.0) | 0.658 |
| Peripheral arteriopathy (n [%]) | 14 (9.6) | 8 (11.4) | 3 (8.3) | 3 (7.5) | 0.763 |
| Previous TIA (n [%]) | 17 (11.6) | 7 (10.0) | 4 (11.1) | 6 (15.0) | 0.729 |
| Dialysis technique before study (n [%]) | | | | | 0.296 |
| HD | 124 (84.9) | 61 (87.1) | 32 (88.9) | 31 (77.5) | |
| HDF | 22 (15.1) | 9 (12.9) | 4 (11.1) | 9 (22.5) | |
| Dialysis vintage (years; median [IQR]) | 3.0 (1.4 to 7.7) | 2.5 (1.2 to 9.0) | 4.1 (1.4 to 7.7) | 3.1 (1.5 to 6.1) | 0.636 |
| Dialysis time (minutes; median [IQR]) | 240 (210 to 240) | 240 (210 to 240) | 240 (210 to 240) | 240 (221 to 240) | 0.650 |
| Net UF (L/session; median [IQR]) | 2.8 (2.5 to 3.4) | 2.9 (2.5 to 3.3) | 2.6 (2.0 to 2.9) | 2.8 (2.5 to 3.7) | 0.055 |
| Net UF (% of dry body wt; median [IQR]) | 4.3 (3.9 to 5.0) | 4.4 (3.9 to 5.0) | 4.2 (3.8 to 4.9) | 4.4 (3.8 to 5.1) | 0.448 |

Caractéristiques des patients (2)

Table 2. Laboratory characteristics of enrolled patients at baseline

| Characteristic | Total (N = 146) | HD (n = 70) | HF (n = 36) | HDF (n = 40) | P |
|----------------------------------|------------------------|------------------------|------------------------|------------------------|-------|
| Urea at start of session (mg/dl) | 170 (145 to 194) | 170 (147 to 195) | 169 (138 to 194) | 169 (146 to 186) | 0.851 |
| Hemoglobin (g/dl) | 11.6 (11.0 to 12.1) | 11.5 (10.9 to 12.1) | 11.5 (10.7 to 11.9) | 11.8 (11.2 to 12.2) | 0.108 |
| Sodemia (mMol/L) | 138.0 (136.5 to 140.5) | 138.0 (136.7 to 140.1) | 138.9 (136.7 to 140.8) | 137.5 (134.7 to 139.5) | 0.113 |
| Kaliemia (mMol/L) | 5.55 (5.21 to 5.99) | 5.58 (5.22 to 5.93) | 5.60 (5.21 to 6.29) | 5.50 (5.19 to 5.79) | 0.654 |
| Bicarbonatemia (mMol/L) | 19.9 (18.7 to 21.7) | 19.9 (18.6 to 22.2) | 19.9 (18.5 to 21.5) | 20.0 (19.0 to 21.4) | 0.889 |
| Calcemia (mMol/L) | 1.14 (1.08 to 1.20) | 1.13 (1.08 to 1.17) | 1.16 (1.11 to 1.20) | 1.17 (1.06 to 1.23) | 0.162 |
| Phosphoremia (mMol/L) | 1.61 (1.32 to 1.85) | 1.59 (1.31 to 1.88) | 1.61 (1.31 to 1.89) | 1.62 (1.39 to 1.81) | 0.926 |
| C-reactive protein (mg/dl) | 0.8 (0.3 to 2.3) | 0.7 (0.3 to 2.2) | 0.7 (0.3 to 2.4) | 0.9 (0.3 to 2.6) | 0.935 |
| Plasma albumin (g/dl) | 3.95 (3.65 to 4.20) | 3.95 (3.59 to 4.20) | 3.90 (3.71 to 4.20) | 3.85 (3.70 to 4.35) | 0.958 |
| Total cholesterol (mg/dl) | 161 (138 to 191) | 160 (138 to 189) | 162 (141 to 188) | 164 (128 to 193) | 0.988 |
| Triglycerides (mg/dl) | 154 (100 to 217) | 162 (115 to 255) | 138 (92 to 200) | 154 (94 to 196) | 0.381 |
| eKt/V | 1.27 (1.14 to 1.42) | 1.28 (1.15 to 1.43) | 1.22 (1.13 to 1.39) | 1.19 (1.14 to 1.40) | 0.317 |
| ePCRn (g/kg per day) | 1.13 (0.97 to 1.28) | 1.15 (1.02 to 1.33) | 1.12 (0.95 to 1.22) | 1.10 (0.96 to 1.25) | 0.425 |

ePCRn, equilibrated protein catabolic rate.

Interventions

- Hemodialyse standard: low-flux dialysat 500 ml/mn
- Hemofiltration: high flux, réinjection/débit sg 1:1
- Hémodiafiltration: high flux, réinjection/débit sg 0.6 + dialysat/réinjection 700 ml/mn
- Séances 3-4.5 hres , débit sg 300-400 ml/mn

Outils statistiques

- Analyse descriptive données entre 3 groupes: variances , Kruskal-Wallis et chi.2
- Analyse BP: -diff fréquence ISH, -diff BP predial, intradial et nombre anti hypertenseurs
- Régression multivariée logistique; 1) recherche prédicteurs ISH, 2) comparaison méthodes Dialyse avec HD référence
- Calcul taille échantillon: 246 patients (drop-out rate 30%): hypothèse 3% réduction absolue ISH avec techniques convectives
- Primary outcome: frequency of ISH

Résultats

Table 4. Intradialytic symptomatic hypotension, BP values, and antihypertensive therapy by phase and treatment groups

| Parameter | Treatment | | | | | | P |
|--|------------------|------------------|------------------|------------------|------------------|------------------|--------|
| | Run-in Phase | | | Evaluation Phase | | | |
| | HD | HF | HDF | HD | HF | HDF | |
| No. of patients | 66 | 31 | 39 | 66 | 31 | 39 | |
| No. of sessions | 2096 | 1203 | 1249 | 11942 | 6502 | 5958 | |
| Sessions with symptomatic hypotension (n [%]) | 148 (7.1) | 118 (9.8) | 132 (10.6) | 939 (7.9) | 523 (8.0) | 309 (5.2) | |
| Symptomatic hypotension variation (%) | | | | +0.8 | -1.8 | -5.4 | <0.001 |
| SBP (mmHg; mean ± SD) | 140.5 ± 17.6 | 139.9 ± 18.0 | 137.3 ± 18.9 | 140.5 ± 15.5 | 137.3 ± 18.6 | 141.5 ± 18.8 | |
| mean difference by phase (mmHg) | | | | -0.0 | -2.6 | +4.2 | 0.038 |
| DBP (mmHg; mean ± SD) | 76.7 ± 10.2 | 75.8 ± 9.8 | 74.5 ± 12.6 | 75.4 ± 9.3 | 72.6 ± 9.4 | 74.7 ± 11.4 | |
| mean difference by phase (mmHg) | | | | -1.3 | -3.2 | +0.2 | 0.096 |
| Heart rate (bits/min; mean ± SD) | 74.5 ± 8.2 | 72.7 ± 6.8 | 74.3 ± 10.4 | 73.9 ± 9.2 | 73.4 ± 6.9 | 75.4 ± 9.0 | |
| mean difference by phase (bits/m) | | | | -0.6 | +0.7 | +0.9 | 0.250 |
| No. of antihypertensive drugs (median [IQR]) | 1.0 (0.0 to 2.0) | 1.0 (0.0 to 2.5) | 1.0 (0.7 to 2.0) | 1.0 (0.0 to 1.8) | 0.9 (0.0 to 2.0) | 1.0 (0.6 to 2.0) | 0.385 |
| Patients treated with antihypertensive drugs (%) | 48.6 | 58.3 | 75.0 | 56.1 | 62.1 | 75.9 | |
| difference by phase (%) | | | | +7.5 | +3.8 | +0.9 | 0.676 |
| Postdialysis body weight (kg; mean ± SD) | 64.9 ± 9.7 | 60.7 ± 10.1 | 65.8 ± 12.9 | 64.8 ± 10.0 | 60.2 ± 10.3 | 65.2 ± 12.9 | |
| mean difference by phase (kg) | | | | -0.1 | -0.5 | -0.6 | 0.508 |
| Net UF (L/session; mean ± SD) | 2.7 ± 0.7 | 2.4 ± 0.7 | 2.9 ± 0.7 | 2.7 ± 0.7 | 2.4 ± 0.7 | 2.9 ± 0.9 | |
| mean difference by phase (L/session) | | | | -0.0 | -0.0 | -0.0 | 0.893 |
| Predialysis sodemia (mEq/L; mean ± SD) | 138.3 ± 3.3 | 138.9 ± 2.9 | 137.3 ± 3.2 | 138.0 ± 3.2 | 138.8 ± 2.8 | 137.3 ± 2.9 | |
| mean difference by phase (mEq/L) | | | | -0.3 | -0.1 | -0.0 | 0.942 |
| Postdialysis sodemia (mEq/L; mean ± SD) | 139.0 ± 3.4 | 139.7 ± 3.0 | 138.7 ± 3.4 | 138.7 ± 3.2 | 139.1 ± 2.6 | 138.8 ± 2.7 | |
| mean difference by phase (mEq/L) | | | | -0.3 | -0.6 | -0.1 | 0.808 |
| ΔSession sodemia (mEq/L; mean ± SD) | 0.7 ± 3.3 | 0.8 ± 2.6 | 1.4 ± 2.8 | 0.7 ± 2.6 | 0.3 ± 1.7 | 1.5 ± 2.1 | |
| mean difference by phase (mEq/L) | | | | -0.0 | -0.5 | -0.1 | 0.848 |

Components of sodium balance (body weight, net UF, pre/post-sodiemia values, and Δpost/presession sodiemia values) were also shown. Intradialytic symptomatic hypotension ameliorated in pre-HF (P = 0.011) and in pre-HDF (P < 0.001) groups compared with the HD group, but predialysis SBP values rose in the pre-HDF group as compared with the other groups (P = 0.038).

Résultats

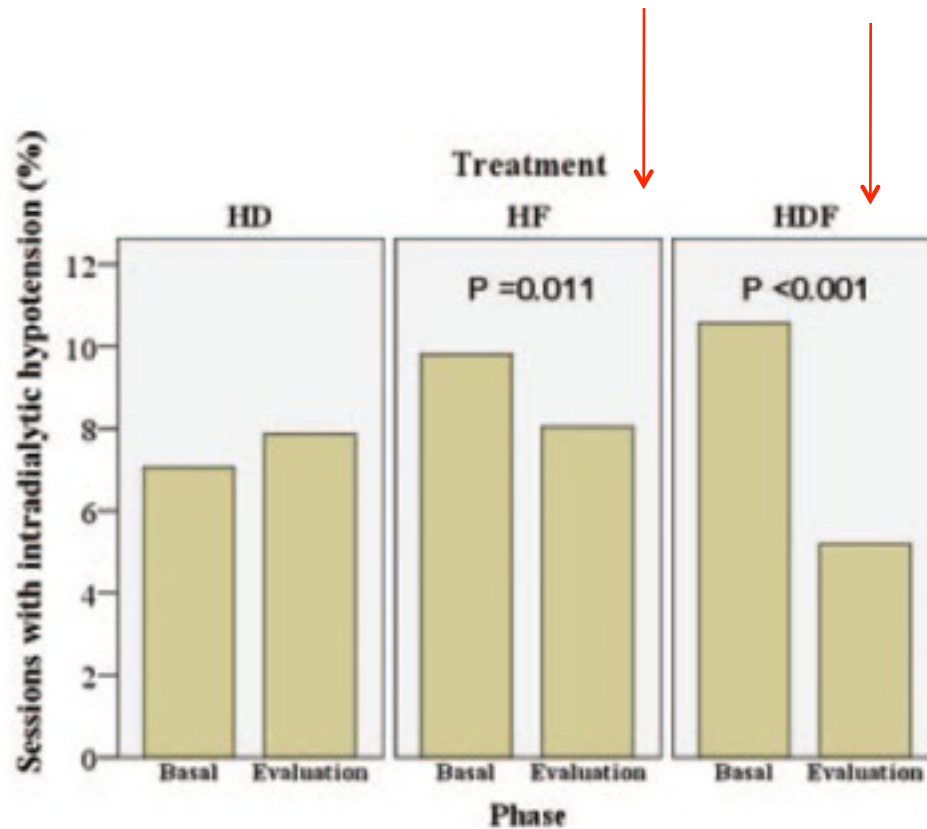


Figure 2. 7.5% of all of the 28,950 sessions were complicated by ISH. In the evaluation period compared with the basal run-in, there was a statistically significant decrease of sessions with ISH in HF (9.8 to 8.0%, decrease of 18.4%; $P = 0.011$) and in HDF (10.6 to 5.2%, decrease of 50.9%; $P < 0.001$) compared with low-flux HD group (7.1 to 7.9%, increase of 9.9%).

Résultats

Table 5. Predictors associated with symptomatic intradialytic hypotension by means of multiple logistic regression

| Parameter | B | P | OR | 95% CI |
|-------------------------------|--------|--------|-------|----------------|
| Diabetes | 0.517 | <0.001 | 1.680 | 1.480 to 1.900 |
| Age (years) | 0.024 | <0.001 | 1.020 | 1.020 to 1.030 |
| SBP (mmHg) | -0.025 | <0.001 | 0.975 | 0.972 to 0.978 |
| DBP (mmHg) | 0.007 | 0.011 | 1.010 | 1.002 to 1.012 |
| Ischemic cardiopathy | 0.493 | <0.001 | 1.640 | 1.470 to 1.830 |
| Chronic ischemic arteriopathy | 0.430 | <0.001 | 1.540 | 1.340 to 1.770 |
| Previous TIA | 0.715 | <0.001 | 2.040 | 1.800 to 2.320 |
| Net UF rate (dl/h) | 0.130 | <0.001 | 1.140 | 1.120 to 1.160 |
| Experimental treatment | | <0.001 | | |
| HF | -0.378 | 0.011 | 0.690 | 0.510 to 0.920 |
| HDF | -0.782 | <0.001 | 0.460 | 0.330 to 0.630 |

This model was applied to a total of 28,950 sessions in run-in and evaluation periods. Overall, symptomatic intradialytic hypotension was present in 7.5% of cases. The beneficial effect of HF and HDF, compared with the reference HD and adjusted for the effect of the other covariates included in the model, was highly significant ($P = 0.011$ and $P < 0.001$, respectively). B, regression coefficient.

Points de la discussion

- Premier RCT sur techniques de dialyse avec stabilité hemodyn comme outcome
- Diminution 54 de la fréquence d'ISH
- A première vue, 0 différence bilan sodé mais pas exclu (predialysis SBP plus hte en HDF)
- Effet liquide reinj online plus froid ?
- Population peu standard ?
- Importantes implications cliniques

Limitations reconnues par auteurs

- Généralisation à toute population en HD
(Prevalence faible diabète , obésité et nb med antiHTA peu important)
- Taille échantillons

Mon impression ...

Bonne étude car:

- RCT, o effet centre, pragmatique, mortalité plus faible avec HDF

Mais

- RCT ciblé sur patients avec ISH fréquente ? ou avec Hypota chronique

Question:

- HDF pour tous ?