
The author declares no conflicting interest
Super high-flux dialyzer and online HDF, Japanese trends and perspective

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Introduction

- It is widely known that the survival rate of Japanese HD patients is the highest in the world.
- This is mainly due to the development of dialysis and blood purification devices and preparation of the dialysis system.
- Cooperation among academic societies, the clinical engineering technologists, and industries has also played a significant role.
- Especially, the introduction of the central dialysis fluid delivery system (CDDS) in the 1960s realized the provision of stable dialysis conditions for all patients, which made a marked contribution.
Introduction

- This favorable survival rate has been achieved by applying standardized dialysis under identical conditions (4-hour, 3 times a week using a super high-flux membrane) at all facilities nationwide.

Japanese standard

- CDDS + Super high-flux (HPM) dialyzers
DOPPS; survival rate of HD

Data from DOPPS I (1997 through 2001). Cox proportional hazards model adjusted for age, male gender, black race, coronary artery disease, congestive heart failure, other cardiac disease, left ventricular hypertrophy, cardiomegaly by x-ray, hypertension, cardiovascular disease, peripheral vascular disease, diabetes, lung disease, dyspnea, smoking, cancer, HIV/AIDS, gastrointestinal bleed, peptic ulcer disease, hepatitis B, hepatitis C, neurologic disorder, psychiatric disease, recurrent cellulitis or gangrene, and vision problems. **P < 0.001.

Robinson, BM and Port, FK. CJASN 4: S12-S17, 2009
Joint; Physician, clinical Engineer & Industry in Japan

Japanese Society for Dialysis Therapy (JSDT)

CDDS
HPM dialyzes

Japan Medical Devices Manufacturers Association

Japan Association of Clinical Engineering Technologists
Dialysis map at 1968 data from JSDT

Total number of bedside console: 110 / 50 facilities
CDDS 28 (56%) facilities

End of 2010
Dialysis bed 118,1352 / 4,152 facilities
Type of modalities of dialysis population

- Day time HD: 82.5% (245,304 people)
- Early night HD: 14.1% (41,914 people)
- Home HD: 0.1% (279 people)
- PD: 3.3% (9,728 people)

JSDT; An overview of regular dialysis treatment in Japan (as of Dec.31, 2010)

Place too much emphasis on Day time center HD
Dialysis center used CDDS
Place too much emphasis on Day time center HD
Advantage and disadvantage of CDDS compared single-patients system

- Advantage
  - Cost effective
  - Maintenance is simple and easy, if the system is placed completely
  - Labor saving of medical staff
  - Automated operation system

- Disadvantage
  - Dialysate composition; no permission to individual
  - Machine dysfunction affects all patients
  - Microbial: risk of long dialysis piping for contaminations
Typical CDDS

- **RO**
  - High pressure / Intermittent work

- **Dialysis water proportional unit**
  - Prefilter
  - Check filter
  - RO
  - Storage tank
  - Municipal water
  - Softener Carbon filter
  - Brine tank
  - Rejection

- **Dialysis concentrate mixing**
  - Bicarbonate
  - Acid
  - Powder to liquid concentrate
  - Proportioning unit
  - Temperature monitor
  - Conductivity monitor
  - Deaeration
  - Dialysate storage tank

- **Patients units**
  - Fluid distribution on piping system

- **Central dialysis fluid proportional unit**
  - Larger tanks

- **ETRF**

Issues of CDDS

- Air contaminant space of concentrate mixing place
- Longer fluid line / stagnation fluid
Newly Design of CDDS

Loop line / continuous flow

Water treatment system

Multiple-patient dialysis fluid supply equipment

Dialysis water tank

Dialysis water looped pipe

Dialysis fluid looped pipe

Endotoxin-retentive filter (ETRF)

RO
Low pressure / Continuous work

Powder-mixing device (B)

Powder-mixing device (A)

*1: Exempl and flushing line for remaining fluid
Current status and preparation of the dialysis fluid delivery system,
*JSHDF, Blood purif 2009 (suppl 1)*

- CDDS condition in Japan
Super high-flux dialyzer
  “high performance membrane (HPM) dialyzer”

- Permeability
- Biocompatibility
Permeability

- The classification of dialyzers refers to five types, classified to a clearance (in vitro) of β2-microglobulin by The Ministry of Health, Labor and Welfare.

- β2microglobulin (in vitro)
  - I < 10 mL/min
  - II < 30 mL/min
  - III < 50 mL/min
  - IV < 70 mL/min
  - V ≥ 70 mL/min

- The so-called ‘super high-flux dialyzer’ of type IV and V are shared over 90% in the market in Japan.
Definition of Permeability of high-flux dialyzer in the world

- High flux
  - UFR > 20 mL/mmHg/hr
  - β2MG sieving coefficient (SC) >0.6
  - β2MG clearance (CL): >14mL/min
  - Classification of γ Type III (include part of type II)

- Super high flux
  - γ type IV (β2MG-CLγ50mL/min)
Relation between UFR and BMG-SC

Super high flux dialyzer
Type VI, V

β2microglobulin-SC

UFR (mL/mmHg/hr)
Hemodiafiltration – A New Era

Editors
H. Kawanishi
A.C. Yamashita

High-Performance Membrane Dialyzers

Editors
A. Saito
H. Kawanishi
A.C. Yamashita
M. Mineshima
Definition of HPM
Saito A, Contribution to nephrology 2011

- **Permeation** of medium and large molecules, including low molecular weight proteins (LMWPs) and a small amount of albumin.

- A small amount of albumin, less than 3 g per session, should be removed because the removal would induce an acceleration of turnover of albumin.

- Membrane biocompatibility

Key words!
Albumin permeable
Relationship between the β2MG and α1MG removal rates and albumin loss in the HD mode of HPM dialyzers.
Central online HDF system

- Selection of HDF in all patient

Mainly, pre-dilution online HDF (60-72 L/session)
Dialyzer performance and dilution method in online HDF

- Convective volume is limited because albumin loss increases.
- The dialyzer and dilution method are selected based on how to separate removed high-molecular solutes from albumin loss.
- Post dilution HDF
  - □ Non-protein-permeable dialyzer
    - ➢ Target: BMG aria
  - □ Protein-permeable dialyzer
    - ➢ Target: higher MW (γ 20kd), increase albumin loss
- Pre dilution HDF
  - □ Protein-permeable dialyzer

Recommend of pre HDF used by protein permeable dialyzer
**Albumin loss in HPM dialyzer**
*Tsuchida K et al., Contrib Nephrol 2011, 173:76-83*

- QB 200 mL/min, QD 500 mL/min, 4 hr

**More than 3 g alb loss in HD, Pre-HDF**
Uremic toxin

Vanholder R et al., Kidney Inter 2003; 63: 1934-1943

Free water-soluble low-molecular-weight solutes

Middle molecules

Protein-bound solutes
Protein-bound solutes (N = 25)
Vanholder R et al., KI 2003; 63: 1934

<table>
<thead>
<tr>
<th>Compound</th>
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<td>Methylglyoxal</td>
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<td>N–(carboxymethyl)lysine</td>
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Removal of Protein-bound solutes
Protein permeable dialyzer and post-HDF
Krieter D, Canaud B et al. NDT 2010;25:212

Dialyzer: PES (protein permeable + -), O_B: 380mL/min, O_D: 500mL/min, 230min
On-line HDF: post 100mL/min

Difficult of Bound
Only Free

Cl, mL/min

BMG (11k) Myo (17.6K)

p-cresyl sulfate: F/T= 0.9/20 mg/L
Indoxyl sulfate: F/T= 0.8/20 mg/L
Protein permeable dialyzer in EU
Meert N, Vanholder R et al., NDT 2011; 26:2624-2630

- PES:DIAPES vs Polynephron, close over
- HD, Pre-HDF, Post-HDF

BMG, 11.8kd
Retinol binding protein, 21.2kd
Protein permeable dialyzer in EU
Meert N, Vanholder R et al., NDT 2011; 26:2624-2630

- DIAPES vs Polynephron, close over

Protein-bound solutes

Indole acetic acide

Indoxylsulphate

P-cresylsulphate

HDF: little effective
Protein permeable dialyzer in EU
Meert N, Vanholder R et al., NDT 2011; 26:2624-2630

- BMG: membrane permeability
- LBP: membrane permeability & convection
- PBS: convection but a little

Prescription in this study
- \( Q_B \): 300 mL/min
- \( Q_D \): HD 500, HDF 800 mL/min
- \( Q_F \): post 72 (18L), pre 145 (36L)

Japanese standard of Pre dilution
- \( Q_F = Q_B \) to 1.5\( Q_B \)
- 60-96 L/session

Diagram:
- Albumin loss
- Higher loss
- Need more
- \( p<0.001 \)
- \( p<0.01 \)
Removal of Protein-bound solutes

- Protein permeable dialyzer: low efficiency?
- Higher volume pre-dilution HDF
  - Dilution effects $\Rightarrow$ increase free fraction?
- Daily HD
  - Daily removal of free fraction
Hemodiafilter in Japan

- The classification of dialyzers refers to five types
  - β2microglobulin (in vitro)
    - I < 10 mL/min
    - II < 30 mL/min
    - III < 50 mL/min
    - IV < 70 mL/min
    - V > 70 mL/min

Hemodiafilter
Hemodiafilter in Japan

- No regulation of efficacy
- Still, using same as HPM dialyzer
- In the future, the performance regulation will be established
Pre-dilution online HDF used by Hemodiafilter in Japan

- $Q_B$ 250, $Q_D$ 600, $Q_S$ 250 mL/min (60L)
- MFX-S, ABH-P

Hemodiafilters need more efficacies
Conclusion

- The reasons of highest survival in Japanese HD were the use of the CDDS and HPM dialyzes based on the cooperation among physician, clinical engineer, and industries.

- Pre dilution online HDF used by protein permeable “HPM” dialyzer have a possibility of higher removal of middle molecules and protein-bund substances.