ACUTE DIALYZER REACTIONS IN THE CURRENT ERA

TWO CASES, LITERATURE REVIEW & MANAGEMENT STRATEGY

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INTRODUCTION

In the last decades of the previous century, acute dialysis reactions were relatively common in patients treated by hemodialysis (HD).

Causes included the use of bio-incompatible, complement-activating dialyzer membranes, ethylene-oxide sterilization of dialyzers inducing IgE mediated hypersensitivity and exposure to polyacrylonitrile (PAN) membranes triggering bradykinin production.

However, even in the current era of more biocompatible dialyzers and the replacement of ETO sterilization with other methods, cases of acute dialyzer reactions continue to be reported, also recently (e.g. Semin. Dial. 29:81-84, 2016, Clin. Nephrol. 83:100-103, 2015).

OBJECTIVES

1. To report 2 recent cases of acute dialyzer reactions;
2. To define characteristics of acute dialyzer reactions in the current era;
3. To increase awareness of acute dialyzer reactions;
4. To define a management strategy in cases of acute dialyzer reactions.

CASE 1

Male, 74 years old, diabetic nephropathy, start HD in February 2012.

Dialyzer: **F8-HPS, polysulfone**, steam sterilized, low flux (Fresenius^{R}).

After 7 months gradually increasing **dyspnoea** in early phase (< 30 min) of dialysis, resulting in **severe attacks:** hypotension - hypoxia - abdominal pain.

Switch to **Sureflux**, **cellulose triacetate**, gamma radiation, low flux (Nipro^{R}): **asymptomatic.**

Intentional rechallenge with **F8-HPS dialyzer**: immediate recurrence of symptoms.

Follow-up on cellulose triacetate dialysis sessions uneventful > 3 years.

CASE 2

Male, 69 years old diabetic nephropathy, start HD in November 2015.

Dialyzer: **F8-HPS, polysulfone**, steam sterilized, low flux (Fresenius^{R}).

At 3rd, 5th, 6th and 9th session episodes of severe unexplained hypotension, nausea and vomiting.

Switch to **Sureflux**, **cellulose triacetate**, gamma radiation, low flux (Nipro^{R}): **asymptomatic.**

Accidental rechallenge with **F8-HPS dialyzer**: severe hypotension after 50 minutes.

Follow-up on cellulose triacetate dialysis sessions uneventful > 6 months.

METHODS

PubMed & Internet search for “acute dialyzer reactions” from January 2005 through December 2015.

RESULTS

Literature : 30 more cases (total number analyzed including our cases: 32).

Characteristics of acute reactions

- **Age** 68.7 years range 34 – 90 years
- **Male** 56.3%

- Early after dialyzer exposure (1st or 2nd exposure) 17/32 (53.1%)
- Late after dialyzer exposure (mean 11 months, range 1-36 months 15/32 (46.9%)
- Reaction < 30 min. into dialysis 24/32 (75.0%)
- Reaction > 30 min. into dialysis 8/32 (25.0%) range 45 – 120 min.

- **Manifestations**

– **Dyspnea**	**69 %**
– **Hypotension**	**66 %**
– **Hypoxia**	**44 %**
– **Bronchospasm**	**25 %**
– **Chest pain**	**22 %**
– Pruritus-urticaria	22 %
– Abdominal complaints	22 %
– **Cardio-respiratory arrest**	**19 %**
– Laryngeal edema	6 %
– Death	6 %

Mainly cardio-respiratory system !

Consistent with diagnosis of anaphylaxis !

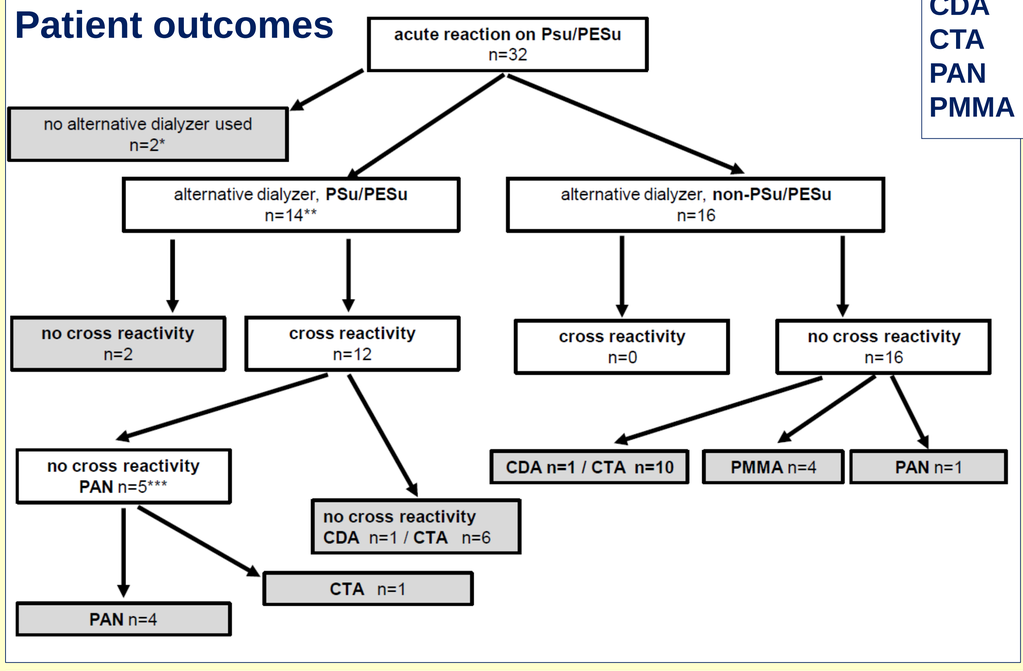
Dialyzers causing acute reactions

- all dialysers contained **polyarylsulfone** membrane
  - **Polysulfone (PSu)** 28 (87.5 %)
  - **Polyethersulfone (PESu)** 4 (12.5 %)

- Fresenius 23 (75.0%) all polysulfone
- Gambro 3 (12.5%) all polyethersulfone
- Toray 3 (12.5%) all polysulfone
- Bbraun 1 (4.2%) polysulfone
- Nipro 1 (4.2%) polyethersulfone
- Asahi 1 (4.2%) polysulfone

Also Bellco-Sorin, Idemsa & Nikkisso in cross-reactions

Patient outcomes



* one patient died, one lost to follow-up
** 11 pts treated with 1 alternative PSu/PESu dialyzer, 2 pts with 2 different PSu/PESu dialyzers, 1 pt with 3 different PSu/PESu dialyzers (= 18 acute reactions)
*** one patient later switched from PAN to CTA because of chronic pruritus / urticaria

Abbreviations

PSu/PESu	polysulfone/polyethersulfone
CDA	cellulose diacetate
CTA	cellulose triacetate
PAN	polyacrilonitrile
PMMA	polymethylmethacrylate

Summary safe dialyzers

membrane	n	%	
CTA/CDA	19	63,3	(17/2)
PAN	5	16,7	
PMMA	4	13,3	
PSu/PEsu	2	6,7	(1/1)

Extensive cross-reactivity between
PSu dialyzers within and among brands
PSu and PESu dialyzers and vice versa
PESu dialyzers among brands

Lost to follow-up: 2 patients

Alternative PSu/PESu dialyzer: 14 patients, 18 trials (see legend to figure)

Only 2 patients (14.3%) could be treated successfully with an alternative PSu/PESu containing dialyzer

In 12 patients (85.7%) or 16 trials (88.9%) acute dialyzer reactions occurred, usually at first exposure

These patients reacted favorably to CTA (n=7), CDA (n=1) or PAN (n=4) dialyzers

Alternative non-PSu/PESu dialyzer: 16 patients

These patients reacted favorably to CTA (n=10), CDA (n=1), PAN (n=1) or PMMA (n=4) dialyzer

CONCLUSIONS

Acute dialyzer reactions in the current era were all caused by dialyzers containing a polysulfone or polyethersulfone capillary membrane.

In ~ 90% of attempts, patients with acute reactions who were treated with a different polysulfone or polyethersulfone dialyzer showed cross-reactivity.

Hence, patients with acute reactions to a polysulfone or polyethersulfone dialyzer should not undergo potentially dangerous exposure to a similar type of dialyzer in a trial-and-error fashion.

They should be switched to a dialyzer containing cellulose triacetate or diacetate (most experience), or to a dialyzer containing polyacrilonitrile (PAN) or polymethylmethacrylate (PMMA).

The incidence of acute dialyzer reactions appears to be low with 32 cases reported in the last decade in which billions of dialyzers have been used world-wide.

However, the true incidence is unknown, many cases not being recognized or remaining unreported.

Consequently, dialysis staff should always consider an acute dialyzer reaction in a patient repeatedly showing unexplained cardio-pulmonary symptoms early during dialysis.

Notably, almost 50% of these reactions occur late (11 months, range 1– 36 months) after first exposure to the offending dialyzer.

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